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XUM

XUM

XUM

# CONTENTS

## General, physical, and inorganic


| NO. | | PAGE |
|---|---|---|
| 1007 | The rôle of supports in catalytic hydrogenation. Part II. Further effects of various oxide supports on the activity of platinum<br>By E. B. Maxted and J. S. Elkins | 5086 |
| 1011. | Substituted benzidines and related compounds as reagents in analytical chemistry. Part XVII. The *NNN'N'*-tetracarboxymethyl derivatives of some 3,3'-disubstituted benzidines<br>By D. I. Rees and W. I. Stephen | 5101 |
| 1012 | The spectra of inorganic complexes in non-aqueous solvents. Part I. Chlorocobaltate ion and cobalt chloride<br>By S. Buffagni and T. M. Dunn | 5105 |
| 1013 | Thermochemical studies. Part VI. Heats and entropies of reaction of transition-metal ions with triethylenetetramine<br>By L. Sacconi, P. Paoletti, and M. Ciampolini | 5115 |
| 1015 | Iodomercurate complexes with Group V quaternary iodides. Part II. Reactions with triphenylphosphine<br>By G. B. Deacon and B. O. West | 5127 |
| 1018 | Manganese(II) chloride complexes. Part I. Stability constants<br>By D. F. C. Morris and E. I. Short | 5148 |
| 1024 | Glow-discharge electrolysis. Part IV. The formation of hydrazine in liquid ammonia<br>By A. Hickling and G. R. Newns | 5177 |
| 1025 | Glow-discharge electrolysis. Part V. The contact glow-discharge electrolysis of liquid ammonia<br>By A. Hickling and G. R. Newns | 5186 |
| 1037 | The crystal structure of monopyridinecopper(II) acetate<br>By G. A. Barclay and C. H. L. Kennard | 5244 |
| 1047 | The polarographic reduction of some heterocyclic molecules. Part III. Quinoline ethiodide<br>By D. J. Casimir, A. J. Harle, and L. E. Lyons | 5297 |
| 1049 | Washburn numbers in the methanol–water–hydrochloric acid system at 25°<br>By D. Feakins | 5308 |
| 1051 | Controlled-potential electrolysis. Part VII. Polarographic behaviour and controlled-potential electrolysis of 1,1-dinitroethane and dinitromethane<br>By Masaichiro Masui and Hiroteru Sayo | 5325 |
| 1061 | The adsorption of water vapour by lecithin and lysolecithin, and the hydration of lysolecithin micelles<br>By P. H. Elworthy | 5385 |
| 1062 | Initial thermoelectric power measurements on thermocells with iodine–iodide electrodes at a mean temperature of 30°<br>By H. J. V. Tyrrell and P. J. Wilson | 5390 |
| 1073 | The gaseous reaction of chlorine trifluoride with methane<br>By C. F. Cullis and C. B. Baddiel | 5449 |
| 1075 | Phosphonitrilic derivatives. Part IX. The crystal structure of octamethylcyclotetraphosphonitrile<br>By Maryon W. Dougill | 5471 |
| 1077 | The rôle of 3*d*-orbitals in π-bonds between (*a*) silicon, phosphorus, sulphur, or chlorine and (*b*) oxygen or nitrogen<br>By D. W. J. Cruickshank | 5486 |
| 1080 | The dielectric polarization of some imperfect polar gases<br>By A. D. Buckingham and R. E. Raab | 5511 |


XUM

NOTES

| NO. | | PAGE |
|---|---|---|
| 1087 | Evidence for a single-stage two-electron exchange in the thallous–thallic reaction<br>By A. G. SYKES | 5549 |
| 1090 | Some reactions of sulphur chloride pentafluoride<br>By A. G. MASSEY and K. J. PACKER | 5554 |

**Physical organic**

| | | |
|---|---|---|
| 1005 | Aromatic reactivity. Part XX. Diphenyl ether, diphenyl sulphide, dibenzofuran, and dibenzothiophen in detritiation<br>By R. BAKER and C. EABORN | 5077 |
| 1006 | Aromatic reactivity. Part XXI. Effects of strongly deactivating substituents in protodetriethylgermylation<br>By C. EABORN and K. C. PANDE | 5082 |
| 1021 | Dipole moments, and absorption spectra of 4-arylazo-1-naphthylamines<br>By D. A. IBBITSON, P. C. JAMES, and R. A. KNAUST | 5163 |
| 1028 | Counter-ion fixation in alginates<br>By A. KATCHALSKY, R. E. COOPER, J. UPADHYAY, and A. WASSERMANN | 5198 |
| 1033 | Studies on uronic acid materials. Part IV. Aqueous decarboxylation of uronic acids, and the decarboxylation of pectic materials during extraction<br>By D. M. W. ANDERSON, A. M. BEWS, S. GARBUTT, and N. J. KING | 5230 |
| 1040 | A comparison of the nucleophilic reactivity of ethoxide, methoxide, and hydroxide ions in dioxan<br>By (MISS) I. R. ALET and B. D. ENGLAND | 5259 |
| 1042 | Quinazolines. Part III. The structure of the hydrated quinazoline cation<br>By ADRIEN ALBERT, W. L. F. ARMAREGO, and E. SPINNER | 5267 |
| 1045 | The kinetics and mechanisms of aromatic halogen substitution. Part XI. Chlorination of phenanthrene in acetic acid<br>By P. B. D. DE LA MARE, N. V. KLASSEN, and R. KOENIGSBERGER | 5285 |
| 1048 | The abstraction of nitric oxide from alkyl nitrites in the vapour phase by methyl radicals<br>By (MRS.) B. BROMBERGER (née JEST) and L. PHILLIPS | 5302 |
| 1050 | Polyanion equilibria in aqueous solution. Part I. The quantitative analysis of acidified tungstate solutions<br>By J. F. DUNCAN and D. L. KEPERT | 5317 |
| 1060 | Physicochemical properties of some chemotherapeutic thioxanthones<br>By D. C. MUNRO | 5381 |
| 1065 | Acylation. Part II. Friedel–Crafts acylation, with stannic chloride as catalyst, in solvents of low dielectric constant<br>By D. P. N. SATCHELL | 5404 |
| 1068 | The mechanism of solvolysis of $\gamma$-phenyltetronic acid enol esters. Part I. A conductometric study of the methanolysis of $\gamma$-phenyltetronic acid enol benzoate<br>By (MRS.) ALICJA M. KIRKIEN-KONASIEWICZ and ALLAN MACCOLL | 5421 |
| 1069 | The solvolysis of $\gamma$-phenyltetronic acid enol esters. Part II. The methanolysis of $\gamma$-phenyltetronic acid enol acetate<br>By (MRS.) ALICJA M. KIRKIEN-KONASIEWICZ | 5430 |
| 1070 | Studies in hydrogen-bond formation. Part X. Complex-formation between a variety of organic solutes in carbon tetrachloride<br>By C. H. GILES, R. B. MCKAY, and (in part) W. GOOD | 5434 |
| 1071 | The pyrolysis of decaborane<br>By A. J. OWEN | 5438 |
| 1076 | Kinetics and mechanism of substitution at the central carbon atom of tri-*p*-nitrophenylmethyl chloride in glacial and aqueous acetic acid<br>By SAUL PATAI and JACOB ZABICKY | 5479 |
| 1078 | The reaction of metals with *o*-phenylenebis(diethylphosphine)<br>By J. CHATT, F. A. HART, and D. T. ROSEVEAR | 5504 |
| 1079 | Some hydrido-complexes of iron(II)<br>By J. CHATT and R. G. HAYTER | 5507 |

| Note no. | | Page |
|---|---|---|
| 1085 | Interaction of boron trichloride with dioxan and 1,3-dioxolan<br>By S. Cooper, M. J. Frazer, and W. Gerrard | 5545 |


## Organic


| | | |
|---|---|---|
| 1003 | Diterpenoid bitter principles. Part III. The constitution of clerodin<br>By D. H. R. Barton, H. T. Cheung, A. D. Cross, L. M. Jackman, and M. Martin-Smith | 5061 |
| 1004 | Condensation of ethyl 2- and 4-pyridylacetate with aromatic carbonyl compounds<br>By D. R. Bragg and D. G. Wibberley | 5074 |
| 1008 | Tanshinones. Part I. The synthesis of an isomer of tanshinone-I<br>By T. J. King and G. Read | 5090 |
| 1009 | Reaction of L-threitol with acetone<br>By A. B. Foster, A. H. Olavesen, and J. M. Webber | 5095 |
| 1010 | The search for chemotherapeutic amidines. Part XIX. 3,3′-Diamidinocarbanilide and its congeners<br>By S. S. Berg | 5097 |
| 1014 | 2-Amino-2-imidazolines and 2-amino-2-oxoazolines<br>By B. Adcock, Alexander Lawson, and D. H. Miles | 5120 |
| 1016 | Pteridine studies. Part XV. The reduction of 2-hydroxypteridine<br>By Adrien Albert and Sadao Matsuura | 5131 |
| 1017 | Heterocyclic compounds from urea derivatives. Part II. Synthesis and cyclisation of 4-substituted 1-amidino-semicarbazides and -thiosemicarbazides<br>By Leonard E. A. Godfrey and Frederick Kurzer | 5137 |
| 1019 | Synthesis of 3-*O*-*p*-coumaroylquinic acid<br>By E. Haslam, R. D. Haworth, and G. K. Makinson | 5153 |
| 1020 | Isomer ratios for the mononitration of *p*-terphenyl in acetic acid and acetic anhydride<br>By G. W. Gray and D. Lewis | 5156 |
| 1022 | Estimation of the relative amounts of isomeric sulphate esters in some sulphated polysaccharides<br>By D. A. Rees | 5168 |
| 1023 | Reactions at position 1 of carbohydrates. Part II. The variation of optical rotation of some aryl glucosides with temperature<br>By B. Capon, W. G. Overend, and M. Sobell | 5172 |
| 1026 | Some derivatives of *S*-(2-hydroxyethyl)thiourea<br>By L. A. Cort | 5191 |
| 1027 | Aucubin<br>By A. J. Birch, J. Grimshaw, and H. R. Juneja | 5194 |
| 1029 | Isatogens. Part I. Base-catalysed condensation products of methyl and ethyl *o*-nitrobenzoylacetate and *o*-nitrobenzoylacetone<br>By R. T. Coutts, M. Hooper, and D. G. Wibberley | 5205 |
| 1030 | Organic reactions in aqueous solution at room temperature. Part II. The influence of pH on condensations involving the linking of carbon to carbon, of carbon to nitrogen, and of carbon to sulphur<br>By J. R. Bethell and P. Maitland | 5211 |
| 1031 | The reaction of nicotinic acid 1-oxide and 3-picoline 1-oxide with acetic anhydride<br>By B. M. Bain and J. E. Saxton | 5216 |
| 1032 | Dehydrogenation with mercuric acetate in the lupane series. Part II. Lupeol and its derivatives<br>By J. M. Allison, William Lawrie, John McLean, and (in part) J. M. Beaton | 5224 |
| 1034 | The composition of *Afraegle paniculata* mucilage<br>By F. G. Torto | 5234 |
| 1035 | Organic peroxides. Part VI. The decomposition of *p*-nitrophenyldiphenylmethyl peroxides<br>By J. I. G. Cadogan, D. H. Hey, and W. A. Sanderson | 5236 |

| NO. | | PAGE |
|---|---|---|
| 1036 | The oxidation of ethers and related compounds. Part I. The thermal and photochemical decomposition of t-butyl peroxide in anisole<br>By H. B. HENBEST, J. A. W. REID, and C. J. M. STIRLING | 5239 |
| 1038 | Experiments confirming the structure of shellolic acid<br>By W. CARRUTHERS, J. W. COOK, (MRS.) N. A. GLEN (née MCGINNIS), and F. D. GUNSTONE | 5251 |
| 1039 | Silyl ethers of tetrahydro-2-hydroxymethylpyran<br>By S. A. BARKER, J. S. BRIMACOMBE, M. R. HARNDEN, and M. STACEY | 5256 |
| 1041 | The hemicelluloses of roselle fibre (*Hibiscus sabdariffa*)<br>By P. C. DAS GUPTA | 5262 |
| 1043 | Essential fatty acids. Part II. Synthesis of (±)-vernolic, linoleic, and γ-linolenic acid<br>By J. M. OSBOND | 5270 |
| 1044 | Bisquaternary salts related to quinapyramine (antrycide). Replacement of the quinoline nucleus by other heterocycles<br>By S. S. BERG and E. W. PARNELL | 5275 |
| 1046 | 1,2-Quinones from derivatives of 2,7-dihydroxynaphthalene<br>By F. BELL | 5293 |
| 1052 | Polysaccharides of the Characeae. Part IV. A non-esterified pectic acid from *Nitella translucens*<br>By D. M. W. ANDERSON and N. J. KING | 5333 |
| 1053 | The oxidation of organic sulphides. Part X. The co-oxidation of sulphides and olefins<br>By D. BARNARD, L. BATEMAN, M. E. CAIN, T. COLCLOUGH, and J. I. CUNNEEN | 5339 |
| 1054 | Synthetic and stereochemical studies in the perhydrobenzocyclohepten-1-one system<br>By DVORA KIMCHI and SHLOMO BIEN | 5345 |
| 1055 | The chemistry of triterpenes and related compounds. Part XLI. The bromination of lupeol and its esters<br>By S. R. GUPTA, T. G. HALSALL, and E. R. H. JONES | 5353 |
| 1056 | Carbonic esters of sucrose. Part I. The preparation of *O*-alkyloxycarbonylsucroses<br>By R. S. THEOBALD | 5359 |
| 1057 | Carbonic esters of sucrose. Part II. The polymerisation of *O*-alkyloxycarbonylsucroses<br>By R. S. THEOBALD | 5365 |
| 1058 | Carbonic esters of sucrose. Part III. The direct preparation of poly(sucrose carbonates) from sucrose<br>By R. S. THEOBALD | 5370 |
| 1059 | The base-catalysed isomerisation of some 3-alkyldihydroanisoles<br>By A. J. BIRCH, (MRS.) E. M. A. SHOUKRY, and F. STANSFIELD | 5376 |
| 1063 | Fungal detoxication. Part V. Metabolism of *o*- and *p*-chlorophenoxyacetic acids by *Aspergillus niger*<br>By J. K. FAULKNER and D. WOODCOCK | 5397 |
| 1064 | Indicine: the major alkaloid of *Heliotropium indicum* L.<br>By (*a*) A. R. MATTOCKS and (MISS) R. SCHOENTAL, and (*b*) (MRS.) H. C. CROWLEY and C. C. J. CULVENOR | 5400 |
| 1066 | Optical rotatory dispersion. Part II. 3-Monohydroxysteroids, 3,17-dihydroxysteroids, and their derivatives<br>By W. KLYNE and P. MARSHALL-JONES. | 5415 |
| 1067 | *N*-Alkylated 5-fluorotryptamines<br>By Z. PELCHOWICZ, A. KALUSZYNER, and M. BENTOV | 5418 |
| 1072 | Structure and stereochemistry of sumatrol and malaccol<br>By L. CROMBIE and R. PEACE | 5445 |
| 1074 | The abnormal hydrolysis of certain β-(diarylphosphino)propionic esters. Part I.<br>By ROY C. HINTON, FREDERICK G. MANN, and DAVID TODD | 5454 |

NO. PAGE

1081 The reactivity of organophosphorus compounds. Part VIII. The reactions of chloroamine-T with triethyl phosphorothiolate and related compounds
By J. I. G. CADOGAN and H. N. MOULDEN . . . . . 5524

1082 The reactivity of organophosphorus compounds. Part IX. The reaction of thionates with alkyl iodides
By A. J. BURN and J. I. G. CADOGAN . . . . . 5532

NOTES

1083 The reactivity of organophosphorus compounds. Part X. The reaction of phosphorothiolates with alkyl iodides
By A. J. BURN, J. I. G. CADOGAN, and H. N. MOULDEN . . . . . 5542

1084 Characterisation of sugars as *p*-*p'*-nitrophenylazobenzoyl derivatives
By EL S. AMIN . . . . . 5544

1086 Thiosuccinimides
By R. J. CREMLYN . . . . . 5547

1088 The thermal isomerization of spirobicyclopropane
By M. C. FLOWERS and H. M. FREY . . . . . 5550

1089 Reactions of sodium 2-oxocyclohexyl thiolsulphate
By BRIAN MILLIGAN and J. M. SWAN . . . . . 5552

1091 Studies of the coal-tar bases. Part IX. A new method of isolation of 2,3-dimethyl- and 2,4,6-trimethyl-pyridine
By R. F. EVANS and W. KYNASTON . . . . . 5556

1092 Indoles. Part VI. Some dioxindoles and their conversion into *o*-aminoaryl ketones
By B. MILLS and K. SCHOFIELD . . . . . 5558

1093 Geometrical isomerism in an azine
By IAN FLEMING and JOHN HARLEY-MASON . . . . . 5560

1094 Diethylsulphonyl-2-(*O*-methyl-α-D-arabopyranosyl)methane and its behaviour with base
By L. HOUGH and A. C. RICHARDSON . . . . . 5561

## INDEX OF AUTHORS' NAMES

ADCOCK, B., Lawson, A., and Miles, D. H., 5120
Albert, A., Armarego, W. L. F., and Spinner, E., 5267
Albert, A., and Matsuura, S., 5131
Alet, I. R., and England, B. D., 5259
Allison, J. M., Lawrie, W., McLean, J., and Beaton, J. M., 5224
Amin, El S., 5544
Armarego, W. L. F. See Albert, A., 5267
Anderson, D. M. W., Bews, A. M., Garbutt, S., and King, N. J., 5230
Anderson, D. M. W., and King, N. J., 5333
Baddiel, C. B. See Cullis, C. F., 5449
Bain, B. M., and Saxton, J. E., 5216
Baker, R., and Eaborn, C., 5077
Barclay, G. A., and Kennard, C. H. L., 5244
Barker, S. A., Brimacombe, J. S., Harnden, M. R., and Stacey, M., 5256
Barnard, D., Bateman, L., Cain, M. E., Colclough, T., and Cunneen, J. I., 5339
Barton, D. H. R., Cheung, H. T., Cross, A. D., Jackman, L. M., and Martin-Smith, M., 5061
Bateman. L. See Barnard, D., 5339
Beaton, J. M. See Allison, J. M., 5224
Bell, F., 5293
Bentov, M. See Pelchowicz, Z., 5418
Berg, S. S., 5097
Berg, S. S., and Parnell, E. W., 5275
Bethell, J. R., and Maitland, P., 5211
Bews, A. M. See Anderson, D. M. W., 5230
Bien, S. See Kimchi, D., 5345
Birch, A. J., Grimshaw, J., and Juneja, H. R., 5194
Birch, A. J., Shoukry, E. M. A., Stansfield, F., 5376
Bragg, D. R., and Wibberley, D. G., 5074
Brimacombe, J. S. See Barker, S. A., 5256
Bromberger, B., and Phillips, L., 5302
Buckingham, A. D., and Raab, R. E., 5511
Buffagni, S., and Dunn, T. M., 5105
Burn, A. J., and Cadogan, J. I. G., 5532
Burn, A. J., Cadogan, J. I. G., and Moulden, H. N., 5542
Cadogan, J. I. G., Hey, D. H., and Sanderson, W. A., 5236
Cadogan, J. I. G., and Moulden, H. N., 5524
Cadogan, J. I. G. See also Burn, A. J., 5532, 5542
Cain, M. E. See Barnard, D., 5339
Capon, B., Overend, W. G., and Sobell, M., 5172
Carruthers, W., Cook, J. W., Glen, N. A., and Gunstone, F. D., 5251
Casimir, D. J., Harle, A. J., and Lyons, L. E., 5297
Chatt, J., Hart, F. A., Rosevear, D. T., 5504
Chatt, J., and Hayter, R. G., 5507

Cheung, H. T. See Barton, D. H. R., 5061
Ciampolini, M. See Sacconi, L., 5115
Colclough, T. See Barnard, D., 5339
Cook, J. W. See Carruthers, W., 5251
Cooper, R. E. See Katchalsky, A., 5198
Cooper, S., Frazer, M. J., and Gerrard, W., 5545
Cort, L. A., 5191
Coutts, R. T., Hooper, M., and Wibberley, D. G., 5205
Cremlyn, R. J., 5547
Crombie, L., and Peace, R., 5445
Cross, A. D. See Barton, D. H. R., 5061
Crowley, H. C. See Mattocks, A. R., 5400
Cruickshank, D. W. J., 5486
Culvenor, C. C. J. See Mattocks, A. R., 5400
Cullis, C. F., and Baddiel, C. B., 5449
Cunneen, J. I. See Barnard, D., 5339
Das Gupta, P. C., 5262
de la Mare, P. B. D., Klassen, N. V., and Koenigsberger, R., 5285
Deacon, G. B., and West, B. O., 5127
Dougill, M. W., 5471
Duncan, J. F., and Kepert, D. L., 5317
Dunn, T. M. See Buffagni, S., 5105
Eaborn, C., and Pande, K. C., 5082
Eaborn, C. See also Baker, R., 5077
Elkins, J. S. See Maxted, E. B., 5086
Elworthy, P. H., 5385
England, B. D. See Alet, I. R., 5259
Evans, R. F., and Kynaston, W., 5556
Faulkner, J. K., and Woodcock, D., 5397
Feakins, D., 5308
Fleming, I., and Harley-Mason, J., 5560
Flowers, M. C., and Frey, H. M., 5550
Foster, A. B., Olavesen, A. H., and Webber, J. M., 5095
Frazer, M. J. See Cooper, S., 5545
Frey, H. M. See Flowers, M. C., 5550
Garbutt, S. See Anderson, D. M. W., 5230
Gerrard, W. See Cooper, S., 5545
Giles, C. H., McKay, R. B., and Good, W., 5434
Glen, N. A. See Carruthers, W., 5251
Godfrey, L. E. A., and Kurzer, F., 5137
Good, W. See Giles, C. H., 5434
Gray, G. W., and Lewis, D., 5156
Grimshaw, J. See Birch, A. J., 5194
Gunstone, F. D. See Carruthers, W., 5251
Gupta, S. R., Halsall, T. G., and Jones, E. R. H., 5353
Halsall, T. G. See Gupta, S. R., 5353
Harle, A. J. See Casimir, D. J., 5297
Harley-Mason, J. See Fleming, I., 5560
Harnden, M. R. See Barker, S. A., 5256
Hart, F. A. See Chatt, J., 5504
Haslam, E., Haworth, R. D., and Makinson, G. K., 5153
Haworth, R. D. See Haslam, E., 5153
Hayter, R. G. See Chatt, J., 5507
Henbest, H. B., Reid, J. A. W., and Stirling, C. J. M., 5239
Hey, D. H. See Cadogan, J. I. G., 5236
Hickling, A., and Newns, G. R., 5177, 5186
Hinton, R. C., Mann, F. G., and Todd, D., 5454
Hooper, M. See Coutts, R. T., 5205
Hough, L., and Richardson, A. C., 5561
Ibbitson, D. A., James, P. C., and Knaust, R. A., 5163
Jackman, L. M. See Barton, D. H. R., 5061
James, P. C. See Ibbitson, D. A., 5163
Jones, E. R. H. See Gupta, S. R., 5353
Juneja, H. R. See Birch, A. J., 5194
Kaluszyner, A. See Pelchowicz, Z., 5418
Katchalsky, A., Cooper, R. E., Upadhyay, J., and Wassermann, A., 5198
Kennard, C. H. L. See Barclay, G. A., 5244
Kepert, D. L. See Duncan, J. F., 5317
Kimchi, D., and Bien, S., 5345
King, N. J. See Anderson, D. M. W., 5230, 5333
King, T. J., and Read, G., 5090
Kirkien-Konasiewicz, A. M., 5430
Kirkien-Konasiewicz, A. M., and Maccoll, A., 5421
Klassen, N. V. See de la Mare, P. B. D., 5285
Klyne, W., and Marshall-Jones, P., 5415
Knaust, R. A. See Ibbitson, D. A., 5163
Koenigsberger, R. See de la Mare, P. B. D., 5285
Kurzer, F. See Godfrey, L. E. A., 5137
Kynaston, W. See Evans, R. F., 5556
Lawrie, W. See Allison, J. M., 5224
Lawson, A. See Adcock, B., 5120
Lewis, D. See Gray, G. W., 5156
Lyons, L. E. See Casimir, D. J., 5297
Maccoll, A. See Kirkien-Konasiewicz, A. M., 5421
McKay, R. B. See Giles, C. H., 5434
McLean, J. See Allison, J. M., 5224
Maitland, P. See Bethell, J. R., 5211
Makinson, G. K. See Haslam, E., 5153
Mann, F. G. See Hinton, R. C., 5454
Marshall-Jones, P. See Klyne, W., 5415
Martin-Smith, M. See Barton, D. H. R., 5061
Massey, A. G., and Packer, K. J., 5554
Masui, M., and Sayo, H., 5325
Matsuura, S. See Albert, A., 5131
Mattocks, A. R., Schoental, R., Crowley, H. C., and Culvenor, C. C. J., 5400
Maxted, E. B., and Elkins, J. S., 5086
Miles, D. H. See Adcock, B., 5120
Milligan, B., and Swan, J. M., 5552
Mills, B., and Schofield, K., 5558
Morris, D. F. C., and Short, E. L., 5148
Moulden, H. N. See Burn, A. J., 5542, and Cadogan, J. I. G., 5524
Munro, D. C., 5381
Newns, G. R. See Hickling, A., 5177, 5186
Olavesen, A. H. See Foster, A. B., 5095
Osbond, J. M., 5270
Overend, W. G. See Capon, B., 5172
Owen, A. J., 5438
Packer, K. J. See Massey, A. G., 5554
Pande, K. C. See Eaborn, C., 5082
Paoletti, P. See Sacconi, L., 5115
Parnell, E. W. See Berg, S. S., 5275
Patai, S., and Zabicky, J., 5479
Peace, R. See Crombie, L., 5445
Pelchowicz, Z., Kaluszyner, A., and Bentov, M., 5418
Phillips, L. See Bromberger, B., 5302
Raab, R. E. See Buckingham, A. D., 5511
Read, G. See King, T. J., 5090
Rees, D. A., 5168
Rees, D. I., and Stephen, W. I., 5101
Reid, J. A. W. See Henbest, H. B., 5239
Richardson, A. C. See Hough, L., 5561
Rosevear, D. T. See Chatt, J., 5504
Sacconi, L., Paoletti, P., and Ciampolini, M., 5115
Sanderson, W. A. See Cadogan, J. I. G., 5236
Satchell, D. P. N., 5404
Saxton, J. E. See Bain, B. M., 5216
Sayo, H. See Masui M., 5325
Schoental, R. See Mattocks, A. R., 5400
Schofield, K. See Mills, B., 5558
Short, E. L. See Morris, D. F. C., 5148
Shoukry, E. M. A. See Birch, A. J., 5376

Sobell, M. See Capon, B., 5172
Spinner, E. See Albert, A., 5267
Stacey, M. See Barker, S. A., 5256
Stansfield, F. See Birch, A. J., 5376
Stephen, W. I. See Rees, D. I., 5101
Stirling, C. J. M. See Henbest, H. B., 5239
Swan, J. M. See Milligan, B., 5552
Sykes, A. G., 5549
Theobald, R. S., 5359, 5365, 5370
Todd, D. See Hinton, R. C., 5454
Torto, F. G., 5234
Tyrrell, H. J. V., and Wilson, P. J., 5390
Upadhyay, J. See Katchalsky, A., 5198
Wassermann, A. See Katchalsky, A., 5198
Webber, J. M. See Foster, A. B., 5095
West, B. O. See Deacon, G. B., 5127
Wibberley, D. G. See Bragg, D. R., 5074, and Coutts, R. T., 5205
Wilson, P. J. See Tyrrell, H. J. V., 5390
Woodcock, D. See Faulkner, J. K., 5397
Zabicky, J. See Patai, S., 5479

XUM

# PAPERS ACCEPTED

Bromo- and iodo-molybdenum(II) compounds. By J. C. SHELDON

Preparation and reactions of dialkylaminoborazoles, and reaction of diethylaminoboron dichloride with primary amines. By W. GERRARD, H. R. HUDSON, and E. F. MOONEY

Some substituted phenethyl and 3-phenylpropyl styryl ketones and the corresponding saturated ketones. By CHRISTINE MAUREEN CLARK and JOHN DOBNEY ANDREW JOHNSON

Reactions of alkoxy-radicals. Part III. Formation of esters from alkyl nitrites. By A. L. J. BECKWITH and G. W. EVANS

Von Braun's " diphenylcyclobutane derivative ": 6,6′-dihydroxy-3,3,3′,3′-tetramethylbis-1,1′-spiroindane and a related compound. By R. F. CURTIS

The electrolysis of some *o*-benzoylbenzoic acids in methanol at 20—30°. By P. J. BUNYAN and D. H. HEY

Studies in relation to biosynthesis. Part XXV. The biosynthesis of ergot alkaloids. By S. BHATTACHARJI, A. J. BIRCH, A. BRACK, A. HOFMANN, H. KOBEL, D. C. C. SMITH, HERCHEL SMITH, and J. WINTER

The hemicelluloses of European larch (*Larix decidua*). Part II. The glucomannan compon. By G. O. ASPINALL, R. BEGBIE, and J. E. MCKAY

The thermal decomposition of dialkyl alkylphosphonates: a new route to alkylphosphonic acids. By A. E. CANAVAN, B. F. DOWDEN, and C. EABORN

The activation of carbon–carbon double bonds by cationic catalysts. Part XI. The interaction of titanium tetrachloride with 1 : 1-diphenylethylene and related compounds in the absence of a co-catalyst. By B. ELLIOTT, ALWYN G. EVANS, and E. D. OWEN

2-Bromomethylnicotinates. Reaction with nucleophilic reagents. By J. HURST and D. G. WIBBERLEY

Phosphonitrilic derivatives. Part VIII. The vibrational spectra of phosphonitrilic halides. By A. C. CHAPMAN and N. L. PADDOCK

Absorption spectra of ketones. Part VII. The $n \longrightarrow \pi^*$ band of axial and equatorial 2-arylcyclohexanones. By R. C. COOKSON and J. HUDEC

Decomposition of ferricinium salts in organic solvents. By R. M. GOLDING and L. E. ORGEL

Complexes formed by α-hydroxy-acid amidines with transition-metal ions. Part I. Acid dissociation constants of the ligands. By R. O. GOULD and R. F. JAMESON

Alkylmercuric derivatives. Oxides, carbonates, and trismethylmercurioxonium salts. By D. GRDENIĆ and F. ZADO

The isotopic exchange reaction of carbonato-cis-diammine(ethylenediamine)cobalt(III) ion and carbonate ion in aqueous solution. By R. A. W. PRATT, E. SHERWIN, and G. J. WESTON

An *X*-ray diffraction determination of the crystal and molecular structure of methyl metadithiophosphonate $[CH_3 \cdot PS_2]_3$. By P. J. WHEATLEY

Reducing reactions of tin(II) in aqueous solution. Part I. A method for the detection of tin(III). By W. C. E. HIGGINSON, R. T. LEIGH, and R. NIGHTINGALE

Reducing reactions of tin(II) in aqueous solution. Part II. The reaction between tin(II) and vanadium(V) in dilute hydrochloric acid. By D. J. DRYE, W. C. HIGGINSON, and P. KNOWLES

The reaction of hexachlorobicyclo[2,2,1]heptadiene with potassium ethoxide. By K. MACKENZIE

Derivatives of stilbenequinone. By WILLIAM BRADLEY and JOHN D. SANDERS

The synthesis of 3-methoxybenz[*a*]anthracene and of 2-methoxynaphthacene. By D. C. C. SMITH

Quinazolines. Part IV. Covalent hydration in the cations of substituted quinazolines. By W. L. F. ARMAREGO

Nucleophilic attacks on carbon–carbon double bond. Part I. General considerations, arylmethylene transfer and cyclodimerisation. By SAUL PATAI and ZVI RAPPOPORT

Nucleophilic attacks on carbon–carbon double bonds. Part II. Cleavage of arylmethylenemalononitriles by water in 95% ethanol. By SAUL PATAI and ZVI RAPPOPORT

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XUM

Small-ring heterocyclic compounds. Part II. Reactions of aliphatic glycidic esters with thiourea and thioacetic acid. By T. C. Owen, C. L. Gladys, and L. Field

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Light-scattering and viscosity studies of two synthetic non-ionic detergents in aqueous solution. By P. H. Elworthy and C. B. Macfarlane

The dissociation constants in water of some bivalent metal alkanedicarboxylates. By R. H. Jones and D. Irwin Stock

Homolytic aromatic substitution. Part XXVII. The reactions of toluene with some para-substituted diaroyl peroxides. By J. K. Hambling, D. H. Hey, and Gareth H. Williams

Gas-phase eliminations. Part III. The pyrolysis of some secondary and tertiary alkyl acetates. By E. U. Emovon and A. Maccoll

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Structural studies of dextrans. Part II. The enzymic synthesis of 3-α-isomaltosylglucose from nigerose. By M. Abdullah, I. J. Goldstein, and W. J. Whelan

The catalytic action of anionic catalysts. Part II. The products of reactions of butyl-lithium with 1,1-diphenylethylene in benzene. By A. G. Evans and D. B. George

Exchange studies of certain chelate compounds of the transitional metals. Part VIII. 2,2′,2″-Terpyridine complexes. By R. Hogg and R. G. Wilkins

The use of thiophen as a chain extender. Part II. Synthetic branched-chain alkanoic acids. By J. F. McGhie, W. A. Ross, D. Evans, and J. E. Tomlin

Akuamma alkaloids. Part V. Akuammine and ψ-akuammigine. By J. A. Joule and G. F. Smith

Formation of stereospecific $DO_2C{\cdot}CHD{\cdot}\dot{C}H{\cdot}CO_2D$ on irradiation of *O,O′*-dideuterosuccinic acid. By D. Pooley and D. H. Whiffen

Stability constants of zinc(II)– and nickel(II)–2,2′-bipyridyl complexes. S. Cabani and M. Landucci

The kinetics and mechanisms of aromatic halogen substitution. Part XIII. Bromination by hypobromous acid in concentrated mineral acids. By P. B. D. de la Mare and I. C. Hilton

Tetrahedral complexes of nickel(II) and the factors determining their formation. Part IV. Complexes with tribenzyl-, dibenzylphenyl-, benzyldiphenyl-, and allyldiphenyl-phosphine. By (Miss) M. C. Browning, J. R. Mellor, D. J. Morgan, S. A. J. Pratt, L. E. Sutton, and L. M. Venanzi

Physicochemical studies on starches. Part XXIV. The fractionation and characterization of starches of various plant origins. By C. T. Greenwood and J. Thomson

The electronic spectra of *N*-heteroaromatic systems. Part IX. $n \longrightarrow \pi$ transitions of polycyclic azines. By S. F. Mason

The liquid hydrogen chloride solvent system. Part IV. Reactions of some compounds containing multiple bonds. By M. E. Peach and T. C. Waddington

The calcium oxide–carbon dioxide system in the pressure range 1—300 atmospheres. By E. H. Baker

The chemistry of colour reactions: the Zimmermann reaction. By T. J. King and C. E. Newall

*N*-Substituted quinolinium ions. Part I. The reactions between the *N*-cyanoquinolinium ion and some nucleophiles. By M. D. Johnson

*N*-Substituted quinolinium ions. Part II. The mechanism of formation of bromoquinolines from the *N*-cyanoquinolinium ion. By M. D. Johnson and J. H. Ridd

Hydropyrimidines. Part I. 1,4,5,6-Tetrahydropyrimidine and its derivatives. By D. J. Brown and R. F. Evans

Synthesis of naphtho [2,3-*b*]thiophen. By W. Carruthers, A. G. Douglas, and James Hill

The conjugated triene acid of *Catalpa ovata* seed oil. By C. Y. Hopkins and Mary J. Chisholm

Carcinogenic nitrogen compounds. Part XXXII. The synthesis of new highly active benzopyridocarbazoles. By Ng Ph. Buu-Hoï, F. Perin, and P. Jacquignon

1,1′-Biphenanthryl and the structure of the oxygenated compound previously so described. By Malcolm Crawford and V. R. Supanekar

The search for new trypanocides. Part VII. *m*-Amidinophenyldiazoaminostyrylquinolinium salts. By S. S. Berg

Triazoles. Part VI. 1,5-diaryl-1,2,4-triazole-3-aldehydes. By (Mrs.) E. J. Browne and J. B. Polya

XUM

The complex ion, $Cr(H_2O)_5NO^{2+}$. By MICHAEL ARDON and JOHN I. HERMAN
Electrical conductance of particles of ion-exchange resin. By J. R. PARRISH
The oxidation of the side chain in kojic acid benzyl ether. By ALAN F. THOMAS
The preparation and properties of new chloride cyanide, and oxygen derivatives of disilane. By ALAN D. CRAIG, JOSEPH V. URENOVITCH, and G. MACDIARMID
Unstable intermediates. Part XIV. The formyl radical. By J. A. BRIVATI, N. KEEN, and M. C. R. SYMONS
Studies in relation to biosynthesis. Part XXVIII. Oxytetracycline (terramycin). By A. J. BIRCH, J. F. SNELL, and (MRS.) P. J. THOMSON
The *O*-alkylation of cyclohexane-1,2-dione. By M. S. GIBSON
Reduction of aromatic nitro-compounds by sodium borohydride catalysed by palladised charcoal. By THOMAS NEILSON, H. C. S. WOOD, and A. G. WYLIE
An improved preparation of methyl 3-amino-α-D-mannoside hydrochloride. By A. C. RICHARDSON
The use of triethylamine in the preparation of *N*-carboxy-L-proline anhydride. By A. A. RANDALL
Constituents of the bark of *Balanops australiana* F. Muell. By C. W. SHOPPEE, M. E. H. HOWDEN, and G. A. R. JOHNSTON
A new reaction of hydrazones. By D. H. R. BARTON, R. E. O'BRIEN, and S. STERNHELL
The crystal structure of $[Co(NO)\{S_2CN(CH_3)_2\}_2]$. By P. R. H. ALDERMAN, P. G. OWSTON, and J. M. ROWE
The thermal reactions of chlorotrifluoroethylene. By B. ATKINSON and M. STEDMAN
Synthetical studies of terpenoids. Part VII. Synthesis of 6,10-dimethyltricyclo[7,2,1,$0^{1,6}$]-dodecan-11-one with the natural configuration of rings. By NITYA GOPLA KUNDU and PHANINDRA CHANDRA DUTTA
The kinetics and mechanisms of additions to olefinic substances. Part VIII. Addition of hypobromous acid to allyl chloride and of hypochlorous acid to allyl bromide. By P. B. D. DE LA MARE, P. C. NAYLOR, and D. L. H. WILLIAMS
The synthesis of disulphides by displacement reactions. By BRIAN MILLIGAN and J. M. SWAN
Reactions of 2-bromoethyl benzilate and 2-bromoethyl mandelate with secondary amines. By G. P. ELLIS, J. KING, and T. B. LEE
Raman effect and solvent extraction. Part III. Spectra of the trichlorostannite and tribromostannite ions. By L. A. WOODWARD and M. J. TAYLOR

# 1003. *Diterpenoid Bitter Principles. Part III.* The Constitution of Clerodin.*[1]

By D. H. R. Barton, H. T. Cheung, A. D. Cross, L. M. Jackman, and M. Martin-Smith.

The bitter principle clerodin (from *Clerodendron infortunatum*) has two acetate residues attached to primary and secondary hydroxyl groups in 1,3-relationship, a vinyl ether system contained in a five-membered ring, a 1,2-epoxide grouping of the type ( ), and an ethereal oxygen atom which is relatively inert. The last is attached to a secondary position and also to the same carbon atom as that to which the oxygen of the cyclic vinyl ether is connected. A relationship between the 1,2-epoxide grouping and the 1,3-glycol system has been demonstrated. Dehydrogenation of clerodin affords 1,2,5-trimethylnaphthalene.

Nuclear magnetic resonance studies are in full agreement with the above facts and, in addition, define further the nature of the cyclic vinyl ether group and the presence of tertiary and secondary methyl groups.

From this evidence the constitution for clerodin determined earlier by *X*-ray crystallography [2] receives strong support. The *X*-ray technique gives the complete relative stereochemistry of the molecule and when this is combined with optical rotatory dispersion measurements reported here the absolute stereochemistry can also be deduced.

Clerodin, the bitter principle of the Indian bhat tree, *Clerodendron infortunatum*, was first isolated by Banerjee,[3] who made a preliminary investigation of the compound and favoured the molecular formula $C_{13}H_{18}O_3$. Chaudhury and Dutta,[4] as a result of further preliminary work, supported a larger molecular formula, $C_{28}H_{40}O_8$.

The constitution and stereochemistry of clerodin have been established as (I; R = Ac) by Sim, Hamor, Paul, and Robertson,[2] using *X*-ray crystallography. The molecular formula, $C_{24}H_{34}O_7$, follows from this work, whilst the molecular weight has been fully confirmed by a mass spectrometric determination kindly carried out by Dr. R. I. Reed at the University of Glasgow. The chemical and nuclear magnetic resonance data that we outline in the sequel provide strong support for the assigned constitution.

Extraction of the ground leaves and twigs of *Clerodendron infortunatum* gave a crude solid from which three crystalline compounds were isolated. All were shown to be closely related. One of the compounds, present in major amount, was clerodin. Preliminary investigation showed that clerodin had two acetate residues, two *C*-methyl groups (Kuhn–Roth), and no methoxyl group. It was readily hydrogenated to a saturated (tetranitromethane test) derivative, which we designate dihydroclerodin-I (II; R = Ac, R′ = R″ = H).† This compound, like clerodin, had no hydroxyl group (infrared), a point about which there had been some confusion earlier.[3,4]

Mild alkaline hydrolysis of clerodin furnished deacetylclerodin (I; R = H), reconverted into clerodin on acetylation. Hydrogenation of deacetylclerodin afforded a saturated dihydro-derivative (II; R = R′ = R″ = H), also available by hydrolysis of dihydroclerodin-I (II; R = Ac, R′ = R″ = H) and reconverted into this by acetylation.

Reduction of dihydroclerodin-I (II; R = Ac, R′ = R″ = H) by lithium aluminium

* The papers by Barton and Elad, *J.*, 1956, 2085, 2090, are regarded as Parts I and II in this series.

† Dihydro-compounds are indicated as series I if the vinyl ether grouping is reduced and as series II if the 1,2-epoxide has been opened.

[1] For a preliminary account see *Proc. Chem. Soc.*, 1961, 76.

[2] Sim, Hamor, Paul, and Robertson, *Proc. Chem. Soc.*, 1961, 75.

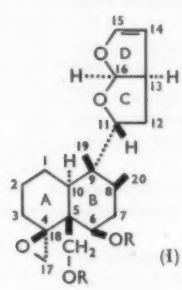
[3] Banerjee, *Science and Culture*, 1936, **2**, 163; *J. Indian Chem. Soc.*, 1937, **14**, 51; *Trans. Bose Res. Inst.*, 1935—1936, **11**, 71; 1936—1937, **12**, 75.

[4] Chaudhury and Dutta, *J. Indian Chem. Soc.*, 1951, **28**, 295; 1954, **31**, 8.

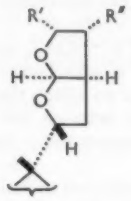


XUM

hydride gave a triol (III; R = R′ = H) which could be reacetylated to a diacetate [tetrahydroclerodin (III; R = R′ = Ac)]. The latter acetate showed hydroxyl absorption in the infrared spectrum but could not be acylated easily and was not oxidised by chromic acid. The new hydroxyl group produced by reduction must, therefore, be tertiary. Similar reduction of clerodin itself gave deacetyldihydroclerodin-II (IV; R = H) which could be readily acetylated to a diacetate (IV; R = Ac), designated dihydroclerodin-II and this, on catalytic hydrogenation, furnished tetrahydroclerodin (III; R = R′ = Ac).



(I)



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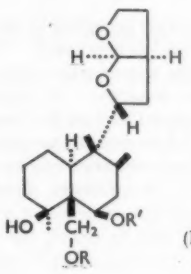

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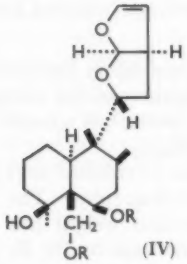

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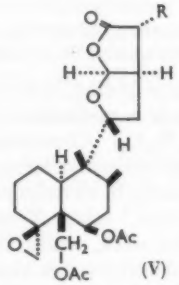

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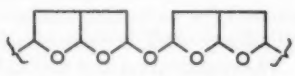


(VI)

Clearly these reduction products are formed by cleavage of an ethereal ring. A 1,2-epoxide always seemed most likely, although a trimethylene oxide ring could not be entirely excluded.[5] Dihydroclerodin-I showed (in $CS_2$) a C–H stretching band at 3045 cm.$^{-1}$ which would support [6] the presence of a 1,2-epoxide. The assignment was confirmed by nuclear magnetic resonance considerations presented below.

Clerodin is very sensitive to acidic conditions and undoubtedly this accounts for some of the difficulties in earlier work. Dissolution in acetic or propionic acid at room temperature converted clerodin into the corresponding hemiacetal esters (II; R = Ac, R′ = OAc or O·CO·Et, R″ = H). Dihydroclerodin-I (II; R = Ac, R′ = R″ = H) itself was inert under these conditions. Treatment of the acetic acid adduct with aqueous acetic acid at room temperature then afforded the hemiacetal (II; R = Ac, R′ = OH, R″ = H), which is the second major crystalline compound from *Clerodendron infortunatum* (see above). The hemiacetal was oxidised smoothly by chromic acid to the γ-lactone (V; R = H) which showed a lactone band at 1795 cm.$^{-1}$. The presence of a five-membered vinyl ether system is thus proved. The acetylated clerodin, m. p. 205°, prepared by Chaudhury and Dutta [4] by the use of acetic anhydride and sodium acetate, is very probably our clerodin hemiacetal acetate (II; R = Ac, R′ = OAc, R″ = H). The configuration at $C_{(15)}$ in all clerodin derivatives is almost certainly α as indicated, for this is the much less hindered orientation.

[5] See Cross, *Proc. Chem. Soc.*, 1960, 344.

[6] Henbest, Meakins, Nicholls, and Taylor, *J.*, 1957, 1459; for tabulated correlations see A. D. Cross, " An Introduction to Practical Infrared Spectroscopy," Butterworths, London, 1960.

The conversion of the hemiacetal of clerodin (II; R = Ac, R′ = OH, R″ = H) into dihydroclerodin-I (II; R = Ac, R′ = R″ = H) was desirable because the former had been isolated in such large quantity (see above) from the plant. We reasoned that toluene-*p*-sulphonation of the hemiacetal should give a derivative (II; R = Ac, R′ = $C_6H_4Me{\cdot}SO_2$, R″ = H) which would at once dissociate to the corresponding oxonium ion. Reduction of the latter *in situ* by sodium borohydride would furnish the desired dihydroclerodin-I (II; R = Ac, R′ = R″ = H). In the event, treatment of the hemiacetal with toluene-*p*-sulphonyl chloride in triethylamine–diethylene glycol dimethyl ether at 0°, followed by addition of the borohydride at −25° to −35°, gave a moderate, but useful, yield of dihydroclerodin-I (II; R = Ac, R′ = R″ = H).

In order to prepare a clerodin derivative containing a " heavy " atom suitable for *X*-ray crystallographic studies the addition of bromine to the vinyl ether system was investigated. Treatment with bromine in acetic acid containing sodium acetate gave smoothly a bromo-acetate (II; R = Ac, R′ = OAc, R″ = Br). Similar reaction with bromine water furnished a bromohydrin (II; R = Ac, R′ = OH, R″ = Br), which was oxidised by chromic acid to the bromo-lactone (V; R = Br) with infrared lactone absorption at 1785 cm.$^{-1}$. It is this compound which was used for the *X*-ray crystallographic study referred to above.

The minor crystalline constituent of *Clerodendron infortunatum* (see above) was found to be the anhydride (VI) of clerodin hemiacetal. The evidence for this unusual structure is briefly as follows. Analysis and molecular-weight determinations suggest a $C_{48}$ formula. Dissolution in aqueous acetic acid gave a high yield (>85%) of clerodin hemiacetal (II; R = Ac, R′ = OH, R″ = H), showing that the two halves of the molecule are identical. Oxidation with chromic acid gave the known γ-lactone (V; R = H) (see above). Reduction with lithium aluminium hydride furnished the corresponding hexaol. Finally the constituent was synthesised by acid-catalysed dehydration of clerodin hemiacetal under mild conditions. We have tried to establish if clerodin hemiacetal and its anhydride are formed from clerodin during storage or in processing. A control experiment with clerodin itself gave no indication of change during our processing procedure. We conclude, therefore, that clerodin hemiacetal and its anhydride may well be true natural products. However, we cannot exclude that they are produced from clerodin during storage in the plant (a period of at least two months) or that some of the other non-crystalline constituents are capable of catalysing the conversion of clerodin into these derivatives.

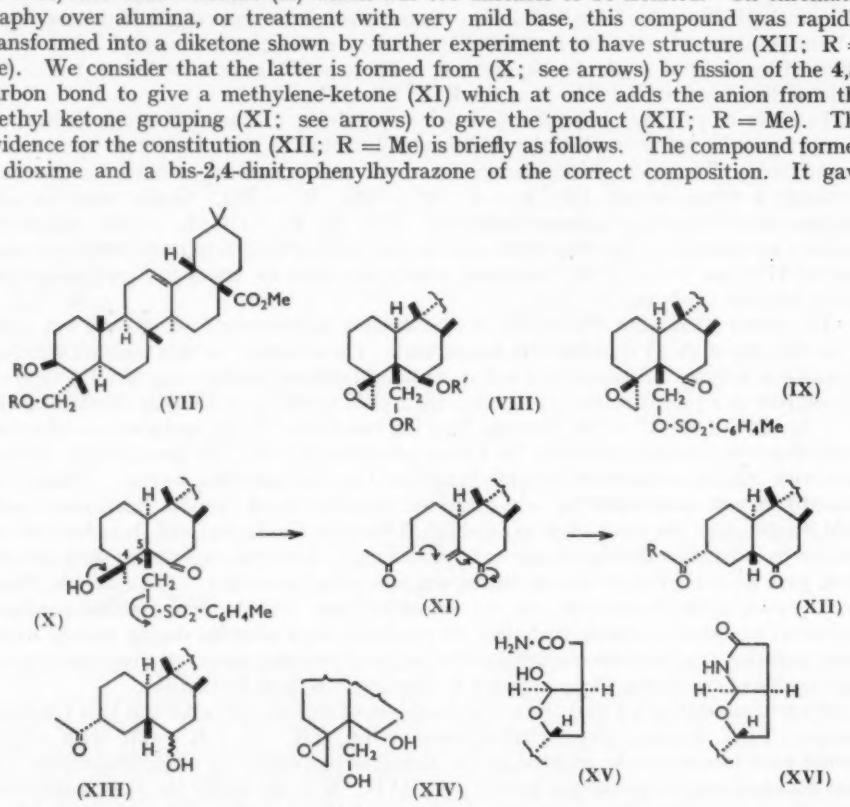
We now present proof that the acetate residues of clerodin are attached to a 1,3-glycol system. First, heating deacetyltetrahydroclerodin (III; R = R′ = H) with copper bronze gave formaldehyde, isolated as the dimedone derivative, in yield comparable with that obtained from hederagenin methyl ester (VII; R = H) under the same conditions. Secondly, treatment of deacetyltetrahydroclerodin (III; R = R′ = H) with ethyl chloroformate in pyridine solution furnished a cyclic carbonate (III; R,R′ = CO). The infrared carbonyl frequency (1735 cm.$^{-1}$) of this compound indicated a six-membered ring and hence derivation from a 1,3-glycol. An analogous carbonate (II; R,R = CO, R′ = R″ = H) was formed in the same way from deacetyldihydroclerodin-I (II; R = R′ = R″ = H). Hederagenin methyl ester, on the other hand, gave only a diethoxycarbonyl derivative [7] (VII; R = $CO_2Et$) under identical conditions. The OH and $CH_2{\cdot}OH$ groups of hederagenin methyl ester are both equatorial but *trans* in configuration. It seems reasonable to assign carbonate formation then to the presence of these two groups (when in 1,3-relationship) in a *cis*-configuration as, in fact, is written into the clerodin formulæ already presented.

The selective reactivity of the two hydroxyl groups of deacetylclerodin derivatives was next investigated with results which eventually determined the relationship between the 1,3-glycol system and the 1,2-epoxide grouping. Deacetyldihydroclerodin-I (II;

[7] Fieser, Herz, Klohs, Romero, and Utne, *J. Amer. Chem. Soc.*, 1952, **74**, 3309.

XUM

R = R′ = R″ = H) on treatment with toluene-*p*-sulphonyl chloride in pyridine readily afforded a monotoluene-*p*-sulphonate (VIII; R = *p*-$C_6H_4Me{\cdot}SO_2$, R′ = H) oxidised by chromic acid to a stable ketone (IX) with a cyclohexanone-type carbonyl band in its infrared spectrum. Deacetyltetrahydroclerodin (III; R = R′ = H), submitted to the same reaction sequence, gave first a monotoluene-*p*-sulphonate (III; R = *p*-$C_6H_4Me{\cdot}SO_2$, R′ = H) and then a ketone (X) which was too unstable to be isolated. On chromatography over alumina, or treatment with very mild base, this compound was rapidly transformed into a diketone shown by further experiment to have structure (XII; R = Me). We consider that the latter is formed from (X; see arrows) by fission of the 4,5-carbon bond to give a methylene-ketone (XI) which at once adds the anion from the methyl ketone grouping (XI; see arrows) to give the product (XII; R = Me). The evidence for the constitution (XII; R = Me) is briefly as follows. The compound formed a dioxime and a bis-2,4-dinitrophenylhydrazone of the correct composition. It gave

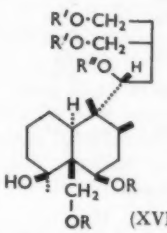



positive iodoform and Zimmermann tests and showed a clear methyl ketone band in its nuclear magnetic resonance spectrum. Controlled hypochlorite oxidation afforded a keto-acid (XII; R = OH). All these compounds had the expected infrared spectra and analytical compositions. Reduction of the diketone with sodium borohydride in excess gave a diol, but reduction under controlled conditions furnished a ketol (XIII). The latter showed a methyl ketone band in its nuclear magnetic resonance spectrum.

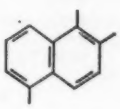
The formation of the diketone (XII; R = Me) is important because it not only proves the presence of the grouping ( ) in clerodin but, on the basis of mechanistic considerations (see above), requires the presence of the partial structure (XIV) (probably contained in two six-membered rings).

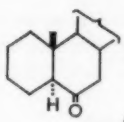
The experiments outlined above define the function of six of the seven oxygen atoms in clerodin. The relationship of the seventh atom to the vinyl ether system was defined in a simple manner. The γ-lactone (V; R = H) from clerodin gave an amide (XV) on treatment with ammonia. Dissolution of this amide in acetic acid at room temperature

afforded a γ-lactam (XVI). Such remarkably ready lactamisation can only be explained if the carbon bearing the " alkyl "-oxygen of the γ-lactone grouping in (V; R = H) is also " acetalic " in character and thus has ethereal oxygen attached to it. The normal fate of the amide (XV) in acetic acid would have been reversion to its lactonic progenitor (V; R = H). This defined one point of attachment for the seventh (ethereal) oxygen atom of clerodin. The other was partially characterised by the following experiments. Prolonged reduction of clerodin hemiacetal (II; R = Ac, R′ = OH, R″ = H) with an excess of lithium aluminium hydride furnished a nicely crystalline hexaol (XVII; R = R′ = R″ = H) which gave a penta-acetate (XVII; R = R′ = R″ = Ac) on acetylation. This derivative retained one hydroxyl group (infrared spectrum) which must be tertiary, because it resisted oxidation by chromic acid. Since the tertiary hydroxyl group formed by opening the 1,2-epoxide group of clerodin has these properties it follows that the two hydroxyl groups resulting from the fission of ring C [see (I)] must both be primary or secondary. With ethyl chloroformate the hexaol gave, first a tetra-acylated derivative (XVII; R,R = CO, R′ = $CO_2Et$, R″ = H) and, on further reaction, a penta-acylated derivative (XVII; R,R = CO, R′ = R″ = $CO_2Et$). The former consumed one atom of oxygen on chromic acid titration, the latter none. The formulæ given explain these facts.



(XVII)


(XVIII)



(XIX)

Evidence for the carbon skeleton of clerodin was obtained by dehydrogenation. This gave 1,2,5-trimethylnaphthalene (XVIII), the derivation of which from structure (I; R = Ac) is obvious.

The relative configurations of clerodin and its derivatives, as written into the formulæ in this paper, are defined by *X*-ray crystallography.[2] The only centre where the assignment is doubtful is $C_{(4)}$. We favour a β-configuration for the oxygen atom of the 1,2-epoxide because tetrahydroclerodin (III; R = R′ = Ac), on dehydration with thionyl chloride or phosphorus oxychloride in pyridine, affords an oily product which shows infrared absorption indicative of $>C=CH_2$. Such a direction of elimination would favour an equatorial hydroxyl group in tetrahydroclerodin [8] and thus a β-configuration. The point is, however, not settled decisively by our experiments.

The absolute configuration which we tentatively favour for clerodin is already written into (I; R = Ac) and derived formulæ. It is based on the following considerations. The ketone toluene-*p*-sulphonate (IX) shows an optical rotatory dispersion curve which, although of enhanced amplitude, is enantiomeric with respect to that of a 6-keto-*trans*-A/B-steroid (as XIX). The same type of curve, but of more normal amplitude, was shown by the keto-acid (XII; R = OH) described above. We thank Professor W. Klyne (Westfield College, University of London) for his kindness in determining these curves.

The biogenesis of clerodin does not call for extended comment. Since the carbon skeleton is the same as that in columbin [9] we can consider that the biogenesis follows the same path as there proposed and thus involves two 1,2-methyl migrations from a diterpenoid skeleton of normal type.

[8] See Barton, Campos-Neves, and Cookson, *J.*, 1956, 3500.
[9] Barton and Elad, *J.*, 1956, 2085, 2090.

XUM

Throughout this investigation we have made extensive use of nuclear magnetic resonance spectroscopy. Conclusions reached on chemical grounds have frequently been anticipated by measurements of this kind and, in addition, further conclusions about the constitution of clerodin can be derived which are not available from our chemical work. Table 1 lists the absorption data for clerodin and a number of its derivatives and the following paragraphs summarise briefly the conclusions reached.

The presence in clerodin of two *C*-methyl groups, in addition to those of the two acetyl residues, follows directly from the integrated intensities of the absorption near 9·0 in all spectra examined. In the spectrum (4) (for numbering see Table 1) of dihydroclerodin-II (IV; R = Ac) the two methyl groups are separately resolved as a singlet and an asymmetric doublet (an $AB_3$ system), thus establishing their attachment to quaternary and tertiary carbon atoms, respectively.

TABLE 1.

Chemical shifts ($\tau$ values) and coupling constants (in parentheses in c./sec.) of protons in clerodin and its derivatives.

| | | Position of Protons | | | | |
|---|---|---|---|---|---|---|
| | Compound | 19 | 20 | O·CO·$CH_3$ | 6 | 11 |
| 1 | (I; R = Ac) | 9·05 | 9·05 | 8·14, 7·98 | *a* | *ca.* 6·1 [a] |
| 2 | (II; R = Ac, R′ = R″ = H) | 9·07 | 9·07 | 8·14, 7·98 | 5·5 [a] | *ca.* 5·8 [a] |
| 3 | (II; R = R′ = R″ = H) | 9·13 | 9·13 | — — | 6·84 | *ca.* 5·8 [a] |
| 4 | (IV; R = Ac) | 8·96 | 9·08 [c] | 7·98, 7·90 | *ca.* 5·5 | 6·10 |
| 5 | (IV; R = H) | 9·04 | 9·04 | — — | 6·2 | *ca.* 6·1 [a] |
| 6 | (III; R = R′ = Ac) | 8·97 | 8·97 | 7·98, 7·91 | *ca.* 5·2 [a] | *ca.* 5·8 [a] |
| 7 | (III; R = R′ = H) | 9·07 | 9·07 | — — | *ca.* 6·2 [a] | *ca.* 5·8 [a] |
| 8 | (V; R = H) | 9·05 | 9·05 | 8·07, 7·91 | *ca.* 5·5 [a] | 5·88 |
| 9 | (XII; R = Me) | 8·87 | 9·09 (7·8) | — — | — | 5·78 [c] |

| | | Position of Protons | | | | |
|---|---|---|---|---|---|---|
| | Compound | 14 | 15 | 16 | 17 | 18 |
| 1 | (I; R = Ac) | *a* | 3·61 (*ca.* 2·5) | 4·09 (6·0) | 7·14 [b] | 5·80, 5·18 (12·8) |
| 2 | (II; R = Ac, R′ = R″ = H) | *a* | 6·15 [c] | 4·51 (4·8) | 7·12 [b] | 5·77, 5·17 (12·4) |
| 3 | (II; R = R′ = R″ = H) | *a* | 6·15 [c] | 4·37 (5·0) | 7·58 [b] | 5·95, 5·67 (12·5) |
| 4 | (IV; R = Ac) | 5·16 (2·5) | 3·53 (2·5) | 4·00 (6·1) | 8·69 | 5·49, 5·13 (12·8) |
| 5 | (IV; R = H) | 5·19 (2·5) | 3·56 (2·5) | 4·01 (6·4) | 8·55 | 5·56 |
| 6 | (III; R = R′ = Ac) | *a* | 6·15 [c] | 4·39 (5·0) | 8·69 | 5·42, 5·05 (12·8) |
| 7 | (III; R = R′ = H) | *a* | 6·15 [c] | 4·41 (5·0) | 8·58 | 5·62 |
| 8 | (V; R = H) | *a* | — | 3·96 (5·6) | *a* | 5·64, 5·14 (12·4) |
| 9 | (XII; R = Me) | *a* | 6·15 [c] | 4·34 (5·0) | 7·86 | — |

*a* Overlapping other absorption. *b* Partially resolved AB system. *c* Complex multiplet.

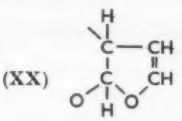
Clerodin (1) and those of its derivatives (2, 3) containing the epoxide ring exhibit absorption in the region 7·2—7·6, typical of the protons of an epoxide. This absorption is absent in compounds (4—7) in which the epoxide ring is reduced, which however exhibit singlets near 8·6, characteristic of a *C*-methyl group in a tertiary alcoholic system. These observations are only explicable in terms of the reduction of a primary epoxide to a tertiary alcohol.[10]

In many spectra (1—7) an unequivocal assignment of lines arising from the absorption of the methylenic protons of the groups $CH_2$·OAc or $CH_2$·OH was possible. In the acetylated compounds the two protons are non-equivalent and the resulting absorptions are AB patterns [11] with the coupling constant, $J$, equal to 12—13 c./sec., a value characteristic of the coupling in an acyclic methylene group. In certain of the free alcohols (5, 7) the methylenic protons attain accidental equivalence, and give rise to a single absorption line. These results prove that the primary acetate group in clerodin is attached to a fully substituted carbon atom.

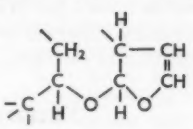
[10] Cf. Tarbell, Carman, Chapman, Huffman, and McCorkindale, *J. Amer. Chem. Soc.*, 1960, **82**, 1005.
[11] L. M. Jackman, "Applications of Nuclear Magnetic Resonance in Organic Chemistry," Pergamon London, 1959, p. 89.

The absorption arising from the α-proton of the secondary acetate (or alcohol) in most compounds overlaps other absorptions, but in the spectra of a number of compounds its approximate position could be inferred from intensity measurements. In deacetyldihydroclerodin-I (II; R = R′ = R″ = H) (3) this proton absorbs at 6·8 compared with *ca.* 6·2 in deacetyltetrahydroclerodin (III; R = R′ = H) (7), suggesting a close steric relation between it and the tertiary alcoholic oxygen atom in the latter compound.

The spectra of clerodin (1) and those derivatives (4, 5) containing the dihydrofuran ring exhibit a triplet ($J$ ~2·5 c./sec.) near 3·6 which can be assigned to the α-olofinic proton since in the spectra (2, 3, 6, 7, 9) of saturated derivatives the band is replaced by another, equivalent to two protons, in the region 6·0—6·3. In the spectra of dihydroclerodin-II (IV; R = Ac) (4) and its deacetyl derivative (5) an identical triplet was also observed at 5·2 and can be assigned to the β-olefinic proton. Convincing evidence for the correctness of these assignments is provided by the proton spectrum of 2,3-dihydrofuran in which the α- and β-olefinic proton absorptions appear as quartets ($J$ = 3·1 c./sec.) at 3·77 and 5·14, respectively. Evidently all coupling constants between the α-, β-, and γ-protons are equal. The spectra (1, 4, 5) of all compounds containing the dihydrofuran ring exhibit a doublet ($J$ = 6·0 — 6·4 c./sec.), equivalent to one proton, at 4·00—4·10. This band is found at 4·30—4·50 with a reduced coupling constant ($J$ = 4·8—5·0 c./sec.) in the spectra (2, 3, 6, 7) of the corresponding dihydro-derivatives, and at 3·96 ($J$ = 5·6 c./sec.) in that of clerodin γ-lactone (V; R = H) (8). Clearly this absorption must be due to the proton at position 16, the paramagnetic shifts associated with the double bond and particularly the carbonyl group being attributable to electron withdrawal from the oxygen atom.[12] The very low τ-values found for this proton require the presence of a second oxygen substituent at position 16 [cf. 3·9—4·6 for the anomeric protons in aldopyranosides[13]], leading to the partial structure (XX). Unequivocal confirmation of



(XX)



(XXI)

structure (XX) was provided by double irradiation experiments * which established that the proton coupled to that at position 16 absorbed at 7·4 (allylic methine) in clerodin and 8·1 (aliphatic methine) in tetrahydroclerodin (III; R = R′ = Ac). The spectrum (9) of the diketone exhibits, in addition to the absorptions of the protons at positions 15 and 16, a double doublet, equivalent to one proton at 5·78. This band must therefore arise from a single proton at position 11. The separations of the inner and outer pairs of lines of this multiplet were field-dependent (determined at 40 and 56·4 Mc./sec.) which identifies it as the X-band of an ABX system. Accordingly, $C_{(11)}$ must be attached to a methylene group and a quaternary carbon atom and the partial structure (XX) can be extended to (XXI).

Several interesting aspects of the chemistry of clerodin did not immediately shed light on its constitution. However, now that the latter is known their significance can be properly evaluated. Treatment of the diketone (XII; R = Me) with potassium t-butoxide in t-butyl alcohol gave, with loss of one molecule of water, an αβ-unsaturated ketone having an ultraviolet maximum at 249 mμ (ε 10,400) and infrared bands indicative of a cyclohexenone. The nuclear magnetic resonance spectrum showed a single peak (τ 3·93) for one vinyl hydrogen atom and the band of the methyl ketone group of (XII; R = Me) had disappeared. For these, and sequential, reasons this enone must be

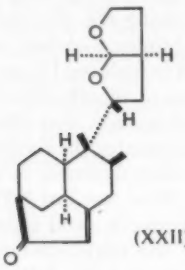
* The technique employed was developed by Dr. D. W. Turner who kindly made the necessary measurements.

[12] Ref. 11, p. 55.

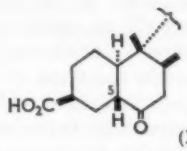
[13] Lemieux, Kullnig, Bernstein, and Schneider, *J. Amer. Chem. Soc.*, 1958, **80**, 6098.

XUM

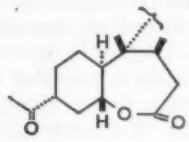
formulated as (XXII). Hydrogenation afforded a cyclohexanone (XXII; double bond reduced) with an infrared carbonyl band at 1710 cm.$^{-1}$. The main proof of constitution was as follows. Ozonolysis of the enone (XXII) gave a crystalline keto-acid in good yield. This was stable to various alkaline treatments and is therefore formulated as the *trans*-derivative (XXIII), epimerisation at $C_{(5)}$ having taken place during the working up.



(XXII)



(XXIII)



(XXIV)

The keto-acid (XXIII) afforded a methyl ester which, when warmed with potassium t-butoxide and then hydrolysed, gave the known keto-acid (XII; R = OH). A *cis*-fusion of rings in (XXII) is, of course, obligatory. Another reaction of the diketone (XII; R = Me) which proceeded in an initially unexpected manner was its behaviour with perphthalic acid. This furnished in a good yield a keto-lactone. This compound is formulated as (XXIV) since it gave a positive iodoform test and showed a methyl ketone band in its nuclear magnetic resonance spectrum. The selective attack of per-acid at the 6-carbonyl group of the diketone (XII; R = Me) parallels the selective reduction by sodium borohydride referred to above (see XIII).

Dr. A. K. Banerjee has kindly informed us [14] that he has also obtained 1,2,5-trimethylnaphthalene by dehydrogenation of clerodin.

## Experimental

M. p.s were taken on the Kofler block. Unless specified to the contrary, $[\alpha]_D$ refer to $CHCl_3$, ultraviolet absorption to EtOH solutions. Nuclear magnetic resonance spectral measurements were made at 21° on approx. 10% w/v solutions in $CDCl_3$ with tetramethylsilane as an internal standard. Spectra were calibrated by the side-band technique with a Muirhead–Wigan decade oscillator model D-695-A. Compounds containing free hydroxyl groups were equilibrated with $D_2O$ before measurements were made. Light petroleum refers to the fraction of b. p. 60—80°, unless stated otherwise. Microanalyses were carried out by Mr. J. M. L. Cameron (Glasgow) and Miss J. Cuckney (Imperial College) and their respective associates.

*Extraction of* Clerodendron infortunatum.—Dry ground leaves and twigs of the shrub (3·5 kg.) were left in ether (14 l.) for 5 days at room temperature with occasional stirring. The filtered ethereal extract was treated twice with charcoal to remove chlorophyll, and the resultant yellow solution concentrated *in vacuo* at <40° to approx. 300 ml. Light petroleum (b. p. 40—60°) (150 ml.) was added cautiously and the solution left at 0°. Crude solid was collected at intervals. The residual solution was again concentrated and the process repeated until no more solid separated (11—20 g. total).

This solid (120 g.) in benzene (250 ml.) was chromatographed over alumina (2·5 kg.; Brockmann grade III). Elution with benzene and with benzene–chloroform mixtures afforded successively a wax (5 g.), clerodin (I; R = Ac) (25 g.), an oil (10 g.), clerodin hemiacetal anhydride (VI) (800 mg.), an oil (40 g.), and clerodin hemiacetal (II; R = Ac, R′ = OH, R″ = H) (30 g.). The non-crystalline products were not investigated further.

Clerodin crystallised from ether–light petroleum (b. p. 40—60°) as needles, m. p. 164—165°, $[\alpha]_D$ −47° (*c* 1·66), ε 4550 at 208 mμ, $\nu_{max.}$ (in Nujol) 1727 and 1252 (acetates), 1615 and 738 (vinyl ether) cm.$^{-1}$, $\nu_{max.}$ (in $CCl_4$) 3025 (olefinic C–H stretch) and 3045 (epoxide) cm.$^{-1}$ (Found:

[14] See Bose, *J. Indian Chem. Soc.*, 1960, **37**, 653.

C, 66·15; H, 7·75; *C*-Me, 15·35; *O*-Me, 0. Calc. for $C_{24}H_{34}O_7$: C, 66·35; H, 7·9; 4*C*-Me, 13·85%).

Clerodin gave a strong yellow colour with tetranitromethane. It was not acetylated by pyridine–acetic anhydride even on the steam bath.

Further reference to clerodin hemiacetal anhydride is made below. Clerodin hemiacetal, recrystallised from ether, proved identical by all criteria with authentic material (see below).

*Deacetylclerodin.*—Clerodin (420 mg.) in methanol (30 ml.) and water (40 ml.) was treated with potassium hydroxide (600 mg.) on the steam bath for 70 min. The saponified product which crystallised was filtered off. Recrystallisation from ethanol gave *deacetylclerodin* (I; R = H) (280 mg.) as prisms, m. p. 230—242°, $[\alpha]_D$ −45° (*c* 0·81 in pyridine), ε 3500 at 209 mμ, $\nu_{max.}$ (in Fluorolube) 1375 cm.$^{-1}$ (singlet only) (Found: C, 69·15; H, 9·05; *C*-Me, 9·2. $C_{20}H_{30}O_5$ requires C, 68·55, H, 8·65; 2*C*-Me, 8·55%). Treatment with pyridine–acetic anhydride for 3 days at room temperature gave back clerodin (m. p., mixed m. p., $[\alpha]_D$, and infrared spectrum).

*Dihydroclerodin-I.*—Clerodin (4·91 g.) in ethyl acetate (100 ml.) was hydrogenated over 5% palladised charcoal (500 mg.) (1 mol. uptake). Crystallisation of the product from ether gave *dihydroclerodin-I* (II; R = Ac, R′ = R″ = H) (4·70 g.) as prisms, m. p. 169—170°, $[\alpha]_D$ −20° (*c* 1·44), no end absorption, $\nu_{max.}$ (in Nujol) 1730 and 1258 and 1224 (acetates) cm.$^{-1}$, $\nu_{max.}$ (in $CCl_4$) 3045 (epoxide) cm.$^{-1}$ (Found: C, 66·25; H, 8·2. $C_{24}H_{36}O_7$ requires C, 66·05; H, 8·3%).

Dihydroclerodin-I (700 mg.) in methanol (20 ml.) was refluxed with potassium hydroxide (1·1 g.) in water (20 ml.) for 2 hr. Chromatography of the oily product over alumina (Grade V) and elution with benzene furnished *deacetyldihydroclerodin-I* (II; R = R′ = R″ = H) as needles (from ether) (190 mg.), m. p. 188—195°, $[\alpha]_D$ −5° (*c* 1·65) (Found: C, 68·45; H, 9·2. $C_{20}H_{32}O_5$ requires C, 68·15; H, 9·15%). The same product (7·1 mg.; m. p., mixed m. p., and infrared spectrum) was formed on hydrogenation of deacetylclerodin (10·1 mg.) in ethyl acetate (10 ml.) over 5% palladised charcoal (25 mg.). Treatment of deacetyldihydroclerodin-I with pyridine–acetic anhydride gave back dihydroclerodin-I (m. p., mixed m. p., and infrared spectrum).

*Clerodin Hemiacetal and its Derivatives.*—Clerodin (400 mg.) in glacial acetic acid (4 ml.) was kept at room temperature until $[\alpha]_D$ was constant (72 hr.). Removal of the solvent *in vacuo* and crystallisation from ether furnished *clerodin hemiacetal acetate* (II; R = Ac, R′ = OAc, R″ = H) (315 mg.) as prisms, m. p. 208—210°, $[\alpha]_D$ +32° (*c* 2·22), no ultraviolet absorption (Found: C, 63·15; H, 7·7; Ac, 26·15. $C_{26}H_{38}O_9$ requires C, 63·15; H, 7·75; 3Ac, 26·1%). The same compound was obtained by acetylation of clerodin with sodium acetate and acetic anhydride according to the directions of Chaudhury and Dutta.[4]

Clerodin (100 mg.) in propionic acid (1 ml.) was kept at room temperature for 72 hr. (constant $[\alpha]_D$). Removal of the solvent *in vacuo* and crystallisation from ether afforded *clerodin hemiacetal propionate* (II; R = Ac, R′ = O·CO·Et, R″ = H) as cubes, m. p. 183—185°, $[\alpha]_D$ 0° (*c* 2·11) (Found: C, 63·7; H, 8·3. $C_{27}H_{40}O_9$ requires C, 63·75; H, 7·95%).

Clerodin hemiacetal acetate (60 mg.) in glacial acetic acid (0·75 ml.) and water (10 ml.) was kept at room temperature for 12 hr. Addition of an excess of sodium hydrogen carbonate, extraction with chloroform, and crystallisation of the product from ether gave *clerodin hemiacetal* (II; R = Ac, R′ = OH, R″ = H) as prisms (32 mg.), m. p. 179—181°, $[\alpha]_D$ −34° (*c* 2·35) (the rotation of −17° given in our preliminary communication is in error), no ultraviolet absorption, $\nu_{max.}$ (in $CS_2$) 3045 (epoxide) cm.$^{-1}$ (Found: C, 63·65; H, 8·2. $C_{24}H_{36}O_8$ requires C, 63·7; H, 8·0%). This hemiacetal (600 mg.) in glacial acetic acid (10 ml.) was treated with sodium dichromate (300 mg.) in the same solvent (10 ml.) overnight. Crystallisation of the product from acetone–light petroleum furnished the *γ-lactone* (V; R = H) (510 mg.) as prisms, m. p. 192—193°, $[\alpha]_D$ −23° (*c* 1·04), no ultraviolet absorption, $\nu_{max.}$ (in $CCl_4$) 1795 (γ-lactone) and 1720 (acetates) cm.$^{-1}$ (Found: C, 63·75; H, 7·85. $C_{24}H_{34}O_8$ requires C, 64·0; H, 7·6%).

Clerodin hemiacetal (II; R = Ac, R′ = OH, R″ = H) (20 g.) and toluene-*p*-sulphonyl chloride (10 g.) in triethylamine (100 ml.) and diethylene glycol dimethyl ether (150 ml.) was kept at 0° for 45 min., then cooled to −25° to −35°. Sodium borohydride (4·17 g.) in the same ether (50 ml.) (at room temperature) was added, and the resulting suspension shaken at −25° to −35° for 2 hr. After addition of water and acidification with cooling, the mixture was extracted with chloroform. The chloroform solution was washed with aqueous alkali and water and then gave a gum which on chromatography over alumina (grade III) gave dihydroclerodin-I (II; R = Ac, R′ = R″ = H) (3·80 g.) and recovered hemiacetal (4·32 g.).

*Clerodin Bromohydrin and its Derivatives.*—Clerodin (515 mg.) in ether (50 ml.) was shaken

XUM

with bromine water added in small portions until the latter was in slight excess. The ethereal solution was washed with sodium hydrogen carbonate solution and worked up in the usual way. Crystallisation of the product from benzene–light petroleum afforded *clerodin bromohydrin* (II; R = Ac, R′ = OH, R″ = Br) as needles (480 mg.), m. p. 186—187° (decomp.), $[\alpha]_D$ −13° (*c* 1·16) (Found: C, 53·6; H, 6·3. $C_{24}H_{35}BrO_8$ requires C, 54·25; H, 6·65%). This bromohydrin (103 mg.) in glacial acetic acid (5 ml.) was treated with sodium dichromate (49 mg.) at room temperature for 90 min. (uptake 1O). Crystallisation of the product from benzene–light petroleum furnished the *bromo-γ-lactone* (V; R = Br) as prisms (82 mg.), m. p. 168—169°, $[\alpha]_D$ −37° (*c* 0·48), no ultraviolet absorption, $\nu_{max.}$ (in Nujol) 1780 (γ-lactone), 1745 (OAc) and 1710 (OAc) cm.$^{-1}$ (Found: C, 54·5; H, 6·3. $C_{24}H_{33}BrO_8$ requires C, 54·45; H, 6·3%).

Clerodin (70 mg.) in glacial acetic acid (4 ml.) was treated with sodium acetate (500 mg.) and bromine (120 mg.) for 90 min. at room temperature. Crystallisation of the product from acetone–light petroleum gave *clerodin bromohydrin acetate* (II; R = Ac, R′ = OAc, R″ = Br) as prisms (75 mg.), m. p. 186—187°, $[\alpha]_D$ +9° (*c* 0·69), $\nu_{max.}$ (in Nujol) 1750 (hemiacetal acetate) and 1730 (acetates) cm.$^{-1}$ (Found: C, 54·6; H, 6·85. $C_{26}H_{37}O_9Br$ requires C, 54·45; H, 6·5%).

*The γ-Lactam* (XVI; R = Ac) *from Clerodin.*—The γ-lactone (V; R = H) (1·04 g.) in methanol (75 ml.) was added to liquid ammonia (50 ml.) at −70° and left for 1 hr. with occasional stirring before being allowed to warm to room temperature. Removal of the solvent *in vacuo* at < 50° and crystallisation from ether furnished the amide (XV; R = Ac) as prisms, m. p. up to 280°, $\nu_{max.}$ (in Nujol) 3535 (OH), 3235 (NH), 1740 and 1715 (acetates) and 1690 (amide-I) cm.$^{-1}$ This amide (100 mg.) in glacial acetic acid (5 ml.) was kept at room temperature for 30 min. before the solvent was removed *in vacuo* at room temperature. Crystallisation of the residue from chloroform–light petroleum (b. p. 40—60°) gave the *γ-lactam* (XVI; R = Ac) as prisms (quantitative yield), m. p. 265—280° (decomp.), $[\alpha]_D$ −6° (*c* 0·81), $\nu_{max.}$ (in Nujol) 3340 (NH), 1740 (acetates), and 1710 (γ-lactam) cm.$^{-1}$ (Found: C, 64·4; H, 8·1; N, 3·15. $C_{24}H_{35}NO_7$ requires C, 64·1; H, 7·85; N, 3·1%).

*Dihydroclerodin-II* (IV; R = Ac).—Clerodin (120 mg.) in dry ether (20 ml.) was refluxed with lithium aluminium hydride (200 mg.) for 16 hr. The product, crystallised from benzene, gave *deacetyldihydroclerodin-II* (IV; R = H) as prisms (62 mg.), m. p. 218—225°, $[\alpha]_D$ −56° (*c* 0·78 in pyridine) (Found: C, 68·9; H, 9·35. $C_{20}H_{32}O_5$ requires C, 68·15; H, 9·15%). Treatment with pyridine–acetic anhydride overnight at room temperature and crystallisation of the product from ether–light petroleum (b. p. 40—60°), furnished *dihydroclerodin-II* (IV; R = Ac) as prisms, m. p. 153—155°, $[\alpha]_D$ −32° (*c* 0·69), $\nu_{max.}$ (in $CCl_4$) 3540 (OH), 1742 (acetates), and 1621 (vinyl ether) cm.$^{-1}$ (Found: C, 66·2; H, 8·4. $C_{24}H_{36}O_7$ requires C, 66·05; H, 8·3%).

*Tetrahydroclerodin* (III; R = R′ = Ac).—Dihydroclerodin-I (700 mg.) in dry ether (50 ml.) was added slowly to lithium aluminium hydride (350 mg.) suspended in the same solvent (20 ml.) under reflux, and refluxing continued for 24 hr. The product, worked up by the potassium hydrogen tartrate method with continuous extraction with chloroform, crystallised from benzene–light petroleum to furnish *deacetyltetrahydroclerodin* (III; R = R′ = H) as prisms (490 mg.), m. p. 172—173°, $[\alpha]_D$ −15° (*c* 1·16) (Found: C, 68·15; H, 9·4. $C_{20}H_{34}O_5$ requires C, 67·75; H, 9·65%). The same compound (m. p., mixed m. p., and infrared spectrum) was obtained by catalytic hydrogenation of deacetyldihydroclerodin-II (IV; R = H) in ethyl acetate over palladised charcoal.

Treatment of deacetyltetrahydroclerodin with pyridine–acetic anhydride overnight at room temperature gave *tetrahydroclerodin* (III; R = R′ = Ac) as prisms (from ether), m. p. 142—147°, $[\alpha]_D$ −6° (*c* 1·10), $\nu_{max.}$ (in $CCl_4$) 3530 (OH) cm.$^{-1}$ (Found: C, 65·7; H, 8·7. $C_{24}H_{38}O_7$ requires C, 65·75; H, 8·75%). The same compound (m. p., mixed m. p., and infrared spectrum) was formed when dihydroclerodin-II (IV; R = Ac) (see above) was hydrogenated in ethyl acetate over palladised charcoal.

Tetrahydroclerodin was recovered unchanged after treatment with sodium dichromate (excess) in glacial acetic acid at room temperature for 24 hr.

*Dehydrogenation of Clerodin.*—Clerodin (750 mg.) was mixed with selenium powder (1·7 g.) and kept at 285—315° under oxygen-free nitrogen for 24 hr. The product, ground to a powder, was exhaustively extracted with ether and then with light petroleum (b. p. 40—60°). The extract, taken up in light petroleum (b. p. 40—60°), was filtered through alumina (grade V) and then extracted with syrupy phosphoric acid to remove azulenic materials. The residual product was then sublimed *in vacuo*, to give a pale yellow oil with an infrared spectrum almost identical with that of authentic 1,2,5-trimethylnaphthalene. The identity was established

by conversion into the 1,3,5-trinitrobenzene adduct and into the picrate and comparison (m. p., mixed m. p., and infrared spectrum) with authentic specimens obtained earlier from onocerin.[15]

*Reduction of Clerodin Hemiacetal* (II; R = Ac, R′ = OH, R″ = H) *with Lithium Aluminium Hydride.*—Clerodin hemiacetal (6·0 g.) in dry dioxan (50 ml.) was added dropwise to a boiling suspension of lithium aluminium hydride (4·5 g.) in the same solvent (50 ml.), and the refluxing continued for 5 days. Ethyl acetate (excess) and water (100 ml.) were added and the organic solvents removed *in vacuo*. Filtration, extraction of the filtrate continuously with chloroform for 48 hr., and crystallisation of the product from acetone–methanol, gave the *hexaol* (XVII; R = R′ = R″ = H) (4·2 g.), prisms, m. p. 146—148°, $[\alpha]_D$ −21° (*c* 0·72 in pyridine), $\nu_{max.}$ (in Nujol) 3300 (OH) cm.$^{-1}$ (Found: C, 64·0; H, 10·05. $C_{20}H_{38}O_6$ requires C, 64·15, H, 10·25%). The hexaol consumed no periodate, but with pyridine–acetic anhydride overnight at room temperature it gave a *penta-acetate* (XVII; R = R′ = R″ = Ac). This did not crystallise even after repeated chromatography; it had b. p. 154—166°/1 × $10^{-5}$ mm., $[\alpha]_D$ −22° (*c* 0·49), $\nu_{max.}$ (in $CHCl_3$) 3570 (OH) and 1742—1727 (5 acetates) cm.$^{-1}$ (Found: C, 61·95; H, 8·3; Ac, 34·35. $C_{30}H_{48}O_{11}$ requires C, 61·65; H, 8·3; 5Ac, 36·8%). The penta-acetate consumed no chromic acid on treatment with sodium dichromate in acetic acid for 20 hr. at room temperature.

The hexaol (700 mg.) in dry pyridine (8 ml.) containing redistilled ethyl chloroformate (3 ml.) was left at 0° for 45 min. Chromatography of the product over alumina (grade V) gave two compounds. Elution with chloroform and crystallisation from benzene–ether afforded the *hexaol carbonate diethoxycarbonyl derivative* (XVII; R,R = CO, R′ = $CO_2Et$, R″ = H) as prisms (390 mg.), m. p. 141—142°, $[\alpha]_D$ −33° (*c* 0·91), $\nu_{max.}$ (in $CHCl_3$) 3350 (OH) and 1745 (carbonate and O·$CO_2$Et) cm.$^{-1}$ (Found: C, 59·45; H, 8·05. $C_{27}H_{44}O_{11}$ requires C, 59·55; H, 8·15%). The earlier fractions from the chromatogram were combined with the mother liquors from the above crystallisation and treated again with ethyl chloroformate. Chromatography of this product gave, besides the derivative reported above, the *carbonate triethoxycarbonyl derivative* (XVII; R,R = CO, R′ = R″ = $CO_2Et$). Crystallised from benzene–ether as needles (60 mg.), this had m. p. 129—130°, $[\alpha]_D$ −38° (*c* 1·04) (Found: C, 58·5; H, 8·0. $C_{30}H_{48}O_{13}$ requires C, 58·4; H, 7·85%). The di- and tri-ethoxycarbonyl derivatives gave a marked m. p. depression on admixture. The former consumed 1O on titration with chromic acid at room temperature, the latter none.

*Characterisation of the* 1,3-*Glycol System in Deacetylclerodin Derivatives.*—(a) *Copper bronze reactions.* Hederagenin methyl ester (80 mg.), mixed with copper bronze (160 mg.), was heated for 2 hr. at 270—300° (metal bath) in a stream of oxygen-free nitrogen which was then passed through saturated aqueous dimedone. After being left for 12 hr. at 0° the formaldehyde dimedone derivative was removed (5·7 mg.) and identified by m. p. and mixed m. p. Under the same conditions deacetyltetrahydroclerodin (85 mg.) gave the formaldehyde dimedone derivative (5·4 mg.), identified by m. p., mixed m. p., and infrared spectrum.

(b) *Reactions with ethyl chloroformate.* Deacetyltetrahydroclerodin (III; R = R′ = H) (50 mg.) in pyridine, when left with an excess of ethyl chlorocarbonate at 0° for 45 min., gave, after chromatography over alumina (grade V) and crystallisation from benzene–light petroleum (b. p. 80—100°), *deacetyltetrahydroclerodin carbonate* (III; R,R′ = CO), prisms, m. p. 226—228°, $[\alpha]_D$ −49° (*c* 0·78), $\nu_{max.}$ (in $CHCl_3$) 3580 and 3400 (OH) and 1735 (carbonate) cm.$^{-1}$ (Found: C, 66·6; H, 8·4. $C_{21}H_{32}O_6$ requires C, 66·3; H, 8·5%).

Deacetyldihydroclerodin-I (70 mg.) was similarly converted into its *carbonate* (II; R,R = CO, R′ = R″ = H). After chromatography over alumina (grade V) and crystallisation from benzene–light petroleum, this formed prisms (32 mg.), m. p. 276—281°, $[\alpha]_D$ −49° (*c* 0·67), $\nu_{max.}$ (in $CHCl_3$) 1739 (carbonate) cm.$^{-1}$, no OH absorption (Found: C, 67·1; H, 8·05. $C_{21}H_{30}O_6$ requires C, 66·65; H, 8·0%).

Hederagenin methyl ester (150 mg.) in the same way gave *di*-O-*ethoxycarbonylhederagenin methyl ester* (VII; R = $CO_2Et$) as prisms (from benzene–methanol), m. p. 172—176°, $[\alpha]_D$ +73° (*c* 1·10), $\nu_{max.}$ (in $CHCl_3$) 1740 (O·$CO_2$Et and Me ester) cm.$^{-1}$ (Found: C, 70·05; H, 9·15. $C_{36}H_{56}O_8$ requires C, 70·1; H, 9·15%).

*Toluene-p-sulphonation of Deacetylclerodin Derivatives.*—Deacetyltetrahydroclerodin (1·445 g.), left with toluene-*p*-sulphonyl chloride (5 mol.) in pyridine (20 ml.) overnight at 0°, gave *deacetyltetrahydroclerodin monotoluene-p-sulphonate* (III; R = *p*-$C_6H_4Me\cdot SO_2$, R′ = H).

[15] Barton and Overton, *J.*, 1955, 2639.

XUM

Recrystallised from benzene–light petroleum, this formed needles (1·94 g.), m. p. 152—153°, $[\alpha]_D$ −8° (*c* 1·06), $\lambda_{max.}$ 225 mμ (ε 13,000), $\nu_{max.}$ (in Nujol) 3300 (OH), 1600, and 1500 (benzene) cm.$^{-1}$ (Found: C, 63·85; H, 7·95. $C_{27}H_{40}O_7S$ requires C, 63·75; H, 7·95%).

*Deacetyldihydroclerodin-I monotoluene*-p-*sulphonate* (VIII; R = *p*-$C_6H_4Me{\cdot}SO_2$, R′ = H), prepared in the same way and crystallised from benzene–light petroleum, had m. p. 149—151°, $[\alpha]_D$ +35° (*c* 1·41) (Found: C, 63·75; H, 7·75. $C_{27}H_{38}O_7S$ requires C, 64·0; H, 7·55%). This monotoluene-*p*-sulphonate (370 mg.) in glacial acetic acid (30 ml.) was treated with sodium dichromate (357 mg.) at room temperature for 38 hr. The product, after chromatography over alumina (grade III) and elution with benzene, afforded the *monoketone ester* (IX). Crystallised from benzene–light petroleum, this formed prisms (120 mg.), m. p. 152—153°, $[\alpha]_D$ +75° (*c* 0·63), $\nu_{max.}$ (in Nujol) 1715 (CO) cm.$^{-1}$ (Found: C, 64·55; H, 7·65. $C_{27}H_{36}O_7S$ requires C, 64·25; H, 7·2%).

*Oxidation of Deacetyltetrahydroclerodin Monotoluene*-p-*sulphonate and Reactions Sequential thereto.*—The monotoluene-*p*-sulphonate (3·01 g.) was treated at room temperature with a four-fold excess of oxidant (sodium dichromate in acetic acid) until one O had been consumed (titrimetric control). The product was worked up at less than 40° and formed a colourless gum with $\lambda_{max.}$ 225 mμ (ε 10,000) and infrared absorption at 3380 (OH) and 1701 (cyclohexanone) cm.$^{-1}$. Chromatography over alumina (grade III) (or treatment with aqueous-ethanolic 2% sodium hydroxide for 1 hr. at room temperature) gave the *diketone* (XII; R = Me). After crystallisation from ether this formed prisms (1·41 g.), m. p. 183—186°, $[\alpha]_D$ +9° (*c* 0·95), $\lambda_{max.}$ 275 mμ (ε 120), $\nu_{max.}$ (in Nujol) 1702 (ketones) cm.$^{-1}$ (Found: C, 71·9; H, 9·35. $C_{30}H_{36}O_4$ requires C, 71·8; H, 9·05%). It gave a negative tetranitromethane test but strongly positive Zimmermann and iodoform reactions.

The diketone furnished a yellow *bis*-2,4-*dinitrophenylhydrazone* as prisms (from acetic acid), m. p. 169—171°, $\lambda_{max.}$ 366 mμ (ε 46,300) (Found: C, 54·95; H, 5·45. $C_{32}H_{38}N_8O_{10}$ requires C, 55·3; H, 5·5%). It also gave a *dioxime*, m. p. 249—251° (from aqueous ethanol), $[\alpha]_D$ −63° (*c* 1·07) (Found: C, 66·35; H, 9·15; N, 7·8. $C_{30}H_{32}N_2O_4$ requires C, 65·9; H, 8·85; N, 7·7%).

Reduction of the diketone (XII; R = Me) (80 mg.) in methanol (4 ml.) at 0° with sodium borohydride (3·0 mg.) in methanol (3 ml.) for 20 min. afforded a product which was separated by chromatography over alumina (grade III) into a diol (7 mg.) (see below) and the *ketol* (XIII) (41 mg.). Crystallised from ether–light petroleum this had m. p. 131—134°, $[\alpha]_D$ +16° (*c* 0·52), $\nu_{max.}$ (in Nujol) 3485 (OH) and 1705 (CO) cm.$^{-1}$ (Found: C, 71·7; H, 9·85. $C_{30}H_{32}O_4$ requires C, 71·4; H, 9·6%).

Reduction of the diketone (30 mg.) in methanol (3 ml.) with sodium borohydride (12 mg.) for 45 min. at room temperature gave the corresponding *diol*. This recrystallised from benzene–light petroleum as prisms (20 mg.), m. p. 163—165°, resolidifying and melting at 172—173°, $[\alpha]_D$ +20° (*c* 0·28), $\nu_{max.}$ (in $CCl_4$) 3310 (OH) cm.$^{-1}$ (Found: C, 70·85; H, 9·85. $C_{30}H_{34}O_4$ requires C, 70·95; H, 10·15%). This diol was identical with the material obtained as a by-product in the selective reduction described above.

The diketone (XII; R = Me) (83 mg.) in ether–chloroform (1 : 1; 10 ml.) containing monoperphthalic acid (4—5 times theor.) was kept at room temperature in the dark for 33 hr. (uptake of one equiv.). Crystallisation of the product from ether–light petroleum (b. p. 40—60°) gave the *keto-lactone* (XXIV) as needles (43 mg.), m. p. 143—145°, $[\alpha]_D$ −6° (*c* 0·47), $\nu_{max.}$ (in Nujol) 1715 (Me ketone and lactone) cm.$^{-1}$ (Found: C, 68·35; H, 9·2. $C_{30}H_{36}O_5$ requires C, 68·55; H, 8·65%). Treatment with aqueous-ethanolic alkali furnished a keto-acid which did not crystallise.

*Treatment of the Diketone* (XII; R = Me) *with Strong Base.*—The diketone (187 mg.) in t-butyl alcohol (11 ml.), made N with potassium t-butoxide, was heated at 50—60° for 1 hr. under oxygen-free nitrogen. Chromatography of the product over alumina (grade V) afforded the *cyclohexenone* (XXII) (140 mg.) as prisms (from benzene–light petroleum), m. p. 177—179°, $[\alpha]_D$ −206° (*c* 0·72), $\lambda_{max.}$ 249 mμ (ε 10,400), $\nu_{max.}$ (in Nujol) 1665 (conjugated ketone) and 1625 (conjugated C:C) cm.$^{-1}$ (Found: C, 75·95; H, 9·15. $C_{29}H_{38}O_3$ requires C, 75·9; H, 8·9%). Hydrogenation of this enone (49 mg.) in ethyl acetate (10 ml.) over 10% palladised charcoal (1 mol. uptake) gave the saturated *ketone* (XXII; saturated) (33 mg.) as plates (from benzene–light petroleum), m. p. 173—175°, $[\alpha]_D$ +57° (*c* 1·07), $\nu_{max.}$ (in $CCl_4$) 1710 (CO) cm.$^{-1}$ [Found: C, 75·6; H, 9·5%; *M* (Rast), 319. $C_{29}H_{40}O_3$ requires C, 75·45; H, 9·5%; *M*, 318].

The cyclohexenone (XXII) (530 mg.) in ethyl acetate (22·5 ml.) and glacial acetic acid (22·5 ml.) was ozonised at 0° for 40 min. (disappearance of ultraviolet band at 249 mμ). The

solvent was removed *in vacuo* and the residue was left in acetic acid (2 ml.) and water (20 ml.) containing 30% hydrogen peroxide (0·5 ml.) for 5 days at room temperature. Crystallisation of the product from chloroform–light petroleum (b. p. 40—60°) gave the *keto-acid* (XXIII) (340 mg.) as needles, m. p. 197—211° (decomp.), $[\alpha]_D$ +12° (*c* 0·30), $\nu_{max.}$ (in Nujol) 3535 (OH), 1740 ($CO_2H$), and 1710 (CO) cm.$^{-1}$ (Found: C, 67·55; H, 8·3. $C_{19}H_{28}O_5$ requires C, 67·85; H, 8·4%). The derived *methyl ester*, prepared with diazomethane in the usual way, crystallised from ether–light petroleum (b. p. 40—60°) as needles, m. p. 130—134°, $[\alpha]_D$ +14° (*c* 0·56), $\nu_{max.}$ (in Nujol) 1725 (ester) and 1700 (CO) cm.$^{-1}$ (Found: C, 68·05; H, 8·3. $C_{20}H_{30}O_5$ requires C, 68·55; H, 8·65%).

The keto-acid (XXIII) was recovered unchanged after treatment with (*a*) 2% sodium hydroxide in aqueous ethanol and (*b*) N-potassium t-butoxide at 55—60° in t-butyl alcohol. The derived methyl ester (25 mg.), kept in N-potassium t-butoxide in t-butyl alcohol (3 ml.) for 30 min. at 55—60° and then, after dilution with water (6 ml.), refluxed for 1½ hr., gave the keto-acid (XII; R = OH). After crystallisation from ether–light petroleum (b. p. 40—60°) the product (needles; 15 mg.) was identified by m. p., mixed m. p., and infrared spectrum.

*Clerodin Hemiacetal Anhydride* (VI).—When recrystallised from ether–light petroleum this *anhydride* (see above) formed prisms, m. p. 210—215°, $[\alpha]_D$ −67° (*c* 1·69), $\nu_{max.}$ (in Nujol) 1735, 1250, and 1225 (acetates) cm.$^{-1}$ (Found: C, 64·6; H, 7·7%; OMe, 0; *M*, 863. $C_{48}H_{70}O_{15}$ requires C, 65·0; H, 7·95%; *M*, 887). From benzene–light petroleum, it formed a *benzene solvate*, m. p. 136—142°, resolidifying and melting at 218—228°, $\lambda_{max.}$ (benzene absorption) 250, 255, and 260 mμ (ε 270, 300, and 240 mμ respectively), $\nu_{max.}$ (in Nujol) 1730, 1255, and 1230 (acetates), 690 (benzene) cm.$^{-1}$ (Found: C, 66·95; H, 7·85. $C_{48}H_{70}O_{15},C_6H_6$ requires C, 67·2; H, 7·95%). Treatment of the anhydride (45 mg.) in acetic acid—water (1 : 1; 1·2 ml.) for 18 hr. at room temperature gave, on crystallisation of the product from ether–light petroleum, clerodin hemiacetal (II; R = Ac, R′ = OH, R″ = H) (39 mg.), identified by m. p., mixed m. p., rotation, and infrared spectrum. Similarly, oxidation of the anhydride (45 mg.) with sodium dichromate dihydrate (66·5 mg.) in glacial acetic acid (5 ml.) at room temperature for 5 hr. gave, after crystallisation from ether–light petroleum, the known γ-lactone, (V; R = H) (23 mg.), identified by m. p., mixed m. p., rotation, and infrared spectrum.

The anhydride (VI) (200 mg.) in ether (100 ml.) was refluxed with lithium aluminium hydride (800 mg.) for 18 hr. The product, crystallised from ethyl acetate–light petroleum (b. p. 40—60°), gave the corresponding *hexaol* (100 mg.) as needles, m. p. 201—209°, $[\alpha]_D$ −76° (*c* 0·45), $\nu_{max.}$ (in Nujol) 3355 (OH) cm.$^{-1}$ (Found: C, 66·1; H, 9·0. $C_{40}H_{66}O_{11}$ requires C, 66·45; H, 9·2%).

Clerodin hemiacetal (583 mg.), moistened with glacial acetic acid (0·3 ml.), was heated at 120° for 5 min.; it liquified. Acetic acid (plus any water formed) was then slowly distilled at 110—125° under gradually reduced pressure (10 mm. to 1 mm.) during 35 min. To the residue were added chloroform and aqueous sodium hydroxide (slight excess). From the chloroform solution there was obtained a gum which, on chromatography over alumina (grade III, neutral), afforded (in order of elution) clerodin (10 mg.), clerodin hemiacetal acetate (55 mg.), clerodin hemiacetal anhydride (VI) (43 mg.), and recovered clerodin hemiacetal (77 mg.). The hemiacetal anhydride obtained was identical (m. p. and mixed m. p. for the unsolvated form and for the benzene adduct; and infrared spectra) with the naturally occurring compound.

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XUM

## 1004. *Condensation of Ethyl 2- and 4-Pyridylacetate with Aromatic Carbonyl Compounds.*

By D. R. Bragg and D. G. Wibberley.

Ethyl 2- and 4-pyridylacetate have been caused to react with a series of aromatic aldehydes in ethanol with piperidine as a catalyst. The normal product was an α-pyridylcinnamate, but *o*-aminobenzaldehyde yielded 3-pyridylquinolin-2-ols and salicylaldehyde yielded 3-pyridylcoumarins. Benzaldehyde has also been condensed with ethyl 2- and 4-pyridylacetate methiodides, the product from the former salt being a derivative of ethyl *cis*-cinnamate; the *trans*-isomer has been obtained by the action of methyl iodide on ethyl α-2′-pyridylcinnamate.

Attempts to condense aromatic ketones with ethyl 2- and 4-pyridylacetate failed, but the methiodide of the latter ester with *o*-aminoacetophenone produced 4-methyl-3-4′-pyridylquinolin-2-ol methiodide.

Ethyl 2- and 4-pyridylacetate have been known since 1936, and methods are available for their preparation in good yield from the corresponding picolines. In spite of this, and of the numerous examples in the literature concerning the condensations of 2- and 4-picolines [1] and of their methiodides, little work appears to have been carried out on the condensations of pyridylacetates with aldehydes or ketones. The only such reactions known to the authors are the condensation by Kakimoto *et al.*[2] of ethyl 4-pyridylacetate with benzaldehyde in the presence of acetic anhydride to yield ethyl α-4′-pyridylcinnamate and that by Hartmann and Bosshard [3] of the sodio-derivative of ethyl 3-pyridylacetate with benzaldehyde to yield ethyl α-3′-pyridylcinnamate. It is well known [4] that whereas 2- and 4-picoline with benzaldehyde give good yields of styrylpyridines only in the presence of acetic anhydride or zinc chloride as catalyst, the corresponding methiodides give excellent yields of the styrylpyridine methiodides by treatment with the aldehyde in boiling alcohol in the presence of piperidine. Roberts [5] suggested that reaction occurs on incipient ionisation of a hydrogen atom of the methyl group. This explains why milder conditions suffice for the methiodides since quaternisation facilitates proton release. Aromatic aldehydes having a strong electron-attracting group in the *ortho*- or *para*-position give better yields than does benzaldehyde in reactions with 2- or 4-picoline but in the piperidine-catalysed reactions of the methiodides, *o*- and *p*-nitrobenzaldehyde, for example, give slightly smaller yields than benzaldehyde; *p*-dimethylaminobenzaldehyde, on the other hand, gives excellent yields with the quaternary salts.[6] Phillips [7] suggested that the dominating factor in condensations involving methiodides is the structure of the final product. He has shown that where the product can be written as a resonating ion in which a major contribution to stability could reasonably be expected from the styryl portion of the molecule, then this product is obtained in excellent yield.

We prepared ethyl 2-pyridylacetate by the method of Woodward and Kornfeld,[8] and ethyl 4-pyridylacetate by Hey and Wibaut's method.[9] In the present work we have shown that these esters condense with aromatic aldehydes in alcohol in presence of piperidine as catalyst, to yield ethyl α-2′- and -4′-pyridylcinnamate. However, aromatic aldehydes having a substituent capable of reaction with the ethoxycarbonyl group gave

[1] Elderfield, "Heterocyclic Compounds," Wiley, New York, 1950, Vol. I, p. 493.
[2] Kakimoto, Nishie, and Yamamoto, *J. Tuberculosis*, 1959, **7**, 76.
[3] Hartmann and Bosshard, *Helv. Chim. Acta*, 1941, **24**, 28.
[4] Ref. 1, p. 496.
[5] Roberts, *Chem. and Ind.*, 1947, 658.
[6] Doja, *J. Indian Chem. Soc.*, 1940, **17**, 347; 1942, **19**, 125.
[7] Phillips, *J. Org. Chem.*, 1947, **12**, 333.
[8] Woodward and Kornfeld, *Org. Synth.*, 1949, **29**, 44.
[9] Hey and Wibaut, *Rec. Trav. chim.*, 1953, **72**, 525.

cyclised products. Thus *o*-aminobenzaldehyde formed 3-2′- and -4′-pyridylquinolin-2-ol, a reaction which may be regarded as an example of the Friedländer synthesis of quinolin-2-ols; and salicylaldehyde yielded 3-2′- and 3-4′-pyridylcoumarin, which may be regarded as a modification of the Perkin coumarin synthesis. The yields varied with the substituents in the aldehyde molecule, being in the sequence 2-OH > 4-$NMe_2$ > H > 2-$NH_2$ > 4-$NO_2$ > 2-$NO_2$, and, with each aldehyde, ethyl 4-pyridylacetate gave a better yield than its 2-isomer. Quaternisation of ethyl 4-pyridylacetate before reaction with *o*-aminoacetophenone afforded 4-methyl-3-4′-pyridylquinolin-2-ol methiodide, where previously no reaction had occurred. The same procedure, however, was not successful with the 2-isomer and neither acetophenone nor *o*-hydroxyacetophenone reacted with ethyl 2- or 4-pyridylacetate or with their methiodides. Quaternisation of the esters before reaction with benzaldehyde did not increase the yields.

From the experiments it may be deduced that electron attraction by the ethoxycarbonyl group increases the incipient ionisation of the methylene group in the pyridylacetic esters to such an extent that the reactions proceed well under the influence of piperidine as catalyst.

Both the *cis*- and the *trans*-form of ethyl α-2′-pyridylcinnamate methiodide have been obtained. Methyl iodide and ethyl α-2′-pyridylcinnamate gave an isomer of the product from benzaldehyde and ethyl 2-pyridylacetate methiodide; the former has a lower m. p. and the principal peak in its ultraviolet absorption curve is at a shorter wavelength, suggesting that the aromatic rings are not co-planar (cf. Braude *et al.*[10]) and this isomer is ethyl *trans*-α-2′-pyridylcinnamate, (*i.e.*, *trans*-cinnamate but *cis*-styrylpyridine).

Horwitz [11] noted a similar phenomenon in condensations of quinaldinium salts with a series of aldehydes, which yield *trans*-2-styrylquinolinium salts having main absorption peaks in the ultraviolet spectra at wavelengths 25—75 mμ longer than those of the *cis*-2-styrylquinolinium salts obtained by condensation of quinaldine with the same aldehydes followed by quaternisation with the appropriate halide or methosulphate. It is unlikely that reaction with methyl iodide affects the configuration of ethyl α-2′-pyridylcinnamate and so it must be assumed that it also has the *trans*-cinnamate configuration.

The bulky methiodide group in ethyl 2-pyridylacetate methiodide has forced a *cis*-cinnamate configuration in its condensation product with benzaldehyde. No such steric effect obtains in ethyl 4-pyridylacetate methiodide and only one isomer, presumably the *trans*-cinnamate, has been obtained by both methods. In the formation of the quinolinols it is not necessary to postulate that *cis*- or *trans*-α-2′-pyridylcinnamates are first formed since cyclisation of the intermediate aldol followed by loss of water from the resulting 3,4-dihydro-4-hydroxyquinolinols and 3,4-dihydro-4-hydroxycoumarins would give the same products.

## Experimental

*General Procedure for Condensation of Ethyl 2- and 4-Pyridylacetate or their Methiodides with Carbonyl Compounds.*—The pyridylacetic ester, or its methiodide (0·01 mol.), the carbonyl compound (0·012 mol.), piperidine (0·5 g.), and ethanol (10·0—15·0 ml.) were refluxed together for 17—18 hr. or, in the case of salicylaldehyde, until the bumping caused by the separated solid became prohibitive. Liquid products were isolated by distillation, and solid products by filtration, after evaporation of the solution to half bulk. Where no crystallisation occurred under these conditions, it was induced in most cases by trituration with water and acetone or alcohol, except for methiodides for which dry ether was used.

*Ethyl* trans-α-2′-*Pyridylcinnamate.*—Ethyl 2-pyridylacetate and benzaldehyde yielded *ethyl* trans-α-2′-*pyridylcinnamate* (46%), b. p. 160—161°/1·0 mm. (Found: C, 75·9; H, 6·0; N, 5·6. $C_{16}H_{15}NO_2$ requires C, 75·9; H, 6·0; N, 5·5%).

*Ethyl* α-4′-*Pyridylcinnamate.*—Ethyl 4-pyridylacetate and benzaldehyde yielded ethyl α-4′-pyridylcinnamate (75%), b. p. 175—176°/2·3 mm. (Found: C, 76·2; H, 6·0; N, 5·6%).

[10] Braude, Jones, Koch, Richardson, Sondheimer, and Toogood, *J.*, 1949, 1890.
[11] Horwitz, *J. Amer. Chem. Soc.*, 1955, **77**, 1687.

XUM

Kakimoto *et al.*[2] obtained the oil in 52% yield, b. p. 190°/3·0 mm., by condensation of the same reactants in the presence of acetic anhydride.

*Ethyl* trans-α-2′-*Pyridylcinnamate Methiodide.*—Ethyl *trans*-α-2′-pyridylcinnamate (0·4 g.) and methyl iodide (5·0 ml.) were refluxed together on the water bath for 2 hr. The mixture was evaporated to give the trans-2-*methiodide* (0·62 g., 100%), m. p. 200—201° (decomp.), which crystallised from ethanol in yellow needles, m. p. 200—201° (decomp.), $\lambda_{max.}$ (in EtOH) 272 mμ (log ε 4·39) (Found: C, 51·9; H, 4·9; N, 3·7. $C_{17}H_{18}INO_2$ requires C, 51·7; H, 4·6; N, 3·8%).

*Ethyl* cis-α-2′-*Pyridylcinnamate Methiodide.*—Ethyl 2-pyridylacetate methiodide, m. p. 81—82° [prepared in quantitative yield by refluxing (2·0 hr.) ethyl 2-pyridylacetate and methyl iodide], and benzaldehyde yielded the cis-2-*methiodide* (35%) which crystallised from ethanol as pale yellow needles, m. p. 227—228° (decomp.), $\lambda_{max.}$ (in ethanol) 331 mμ (log ε 4·17) (Found: C, 51·9; H, 4·3; N, 3·8%). The mixed m. p. with the *trans*-2-methiodide was 192—196°.

*Ethyl* α-4′-*Pyridylcinnamate Methiodide.*—(*a*) Ethyl α-4′-pyridylcinnamate (1·2 g.) and methyl iodide (10·0 ml.) were refluxed on the water bath for 2 hr. to give the 4-*methiodide* (1·87 g., 100%), m. p. 195—197° (decomp.), which separated from ethanol as bright yellow prisms, m. p. 197—198° (decomp.), $\lambda_{max.}$ (in EtOH) 262 mμ (log ε 4·13) (Found: C, 52·0; H, 4·6; N, 3·5%).

(*b*) Ethyl 4-pyridylacetate methiodide (prepared in quantitative yield), m. p. 103—104°, with benzaldehyde yielded the 4-methiodide (42%) which crystallised from ethanol as bright yellow prisms, m. p. 197—198° (decomp.) alone and on admixture with the product from (*a*) (Found: C, 51·5; H, 4·6; N, 3·7%).

*Ethyl* p-*Dimethylamino*-α-2′-*pyridylcinnamate.*—Ethyl 2-pyridylacetate and *p*-dimethylaminobenzaldehyde yielded *ethyl* p-*dimethylamino*-α-2′-*pyridylcinnamate* (76%), which crystallised from aqueous acetone as deep yellow needles, m. p. 127—128° (Found: C, 73·2; H, 6·6; N, 9·5. $C_{18}H_{20}N_2O_2$ requires C, 72·9; H, 6·8; N, 9·45%).

Ethyl 4-pyridylacetate and *p*-dimethylaminobenzaldehyde yielded *ethyl* p-*dimethylamino*-α-4′-*pyridylcinnamate* (89%), which crystallised from aqueous ethanol as deep yellow needles, m. p. 101—102° (Found: C, 73·5; H, 7·0; N, 9·4%).

*Ethyl* 2-*Nitro*-α-4′-*pyridylcinnamate Hydrochloride.*—Ethyl 4-pyridylacetate reacted with *o*-nitrobenzaldehyde in the normal manner. The resulting brown solution was evaporated to dryness and stirred with a mixture of dilute hydrochloric acid and chloroform. Basification of the acidic layer gave only a slight precipitate but evaporation of the chloroform layer gave a semi-solid residue from which the *hydrochloride* (4·2%) was isolated by trituration with acetone. Crystallisation from acetone–ethanol gave needles, m. p. 183—184° (decomp.) (Found: Cl, 10·7; N, 8·5. $C_{16}H_{15}ClN_2O_4$ requires Cl, 10·6; N, 8·4%).

A similar condensation with *p*-nitrobenzaldehyde gave the corresponding 4-*nitro-hydrochloride* (13%) as needles (from acetone), m. p. 147—149° (decomp.) (Found: Cl, 10·6; N, 8·4%). *p*-Nitrobenzaldehyde (80%), m. p. 105—106°, was recovered.

3-2′-*Pyridylquinolin*-2-*ol.*—Ethyl 2-pyridylacetate and *o*-aminobenzaldehyde yielded 3-2′-*pyridylquinolin*-2-*ol* (30%) which crystallised from ethanol as needles, m. p. 236—237°, $\lambda_{max.}$ (in EtOH) 300 mμ, 351 mμ (log ε 4·07, 4·04) (Found: C, 75·7; H, 4·4; N, 12·8%; equiv., 220. $C_{14}H_{10}N_2O$ requires C, 75·7; H, 4·5; N, 12·7%; equiv., 222). By addition of water to the mother liquor an unidentified by-product (0·6 g.) was obtained which crystallised from alcohol as needles, m. p. 137—138°.

3-4′-*Pyridylquinolin*-2-*ol.*—Ethyl 4-pyridyl acetate and *o*-aminobenzaldehyde yielded 3-4′-*pyridylquinolin*-2-*ol* (44%) which crystallised from aqueous ethanol as needles, m. p. 234—235°, $\lambda_{max.}$ (in EtOH) 294, 349 mμ (log ε 4·15, 4·01) (Found: C, 75·7; H, 4·6; N, 12·8%; equiv., 218). The mixed m. p. with the 2-isomer was 218—224°. By addition of water to the mother liquor a by-product (0·55 g.) was obtained which crystallised from ethanol as needles, m. p. 137—138° alone and on admixture with the by-product above.

4-*Methyl*-3-4′-*pyridylquinolin*-2-*ol Methiodide.*—Ethyl 4-pyridylacetate methiodide and *o*-aminoacetophenone yielded 4-*methyl*-3-4′-*pyridylquinolin*-2-*ol methiodide* (17%) which crystallised from aqueous ethanol as pale yellow needles, m. p. 315—316° (decomp.) (Found: C, 50·6; H, 3·9; N, 7·7. $C_{16}H_{15}IN_2O$ requires C, 50·8; H, 4·0; N, 7·4%).

3-2′-*Pyridylcoumarin.*—Ethyl 2-pyridylacetate and salicylaldehyde in 7 hr. at the b. p. yielded 3-2′-*pyridylcoumarin* (75%), which crystallised from ethanol as needles, m. p. 141—142° (Found: C, 75·3; H, 4·1; N, 6·2%; equiv., 227. $C_{14}H_9NO_2$ requires C, 75·35; H, 4·1; N, 6·3%; equiv., 223).

**3-4′-*Pyridylcoumarin*.**—Ethyl 4-pyridylacetate and salicylaldehyde in 2 hr. at the b. p. yielded **3-4′-*pyridylcoumarin*** (94%) which crystallised from ethanol as needles, m. p. 228—229° (Found: C, 75·4; H, 4·2; N, 6·3%, equiv., 214).

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## 1005. *Aromatic Reactivity. Part XX.*[1] *Diphenyl Ether, Diphenyl Sulphide, Dibenzofuran, and Dibenzothiophen in Detritiation.*

By R. BAKER and C. EABORN.

We have measured the rates of detritiation of [2- and 4-$^3H_1$]-diphenyl ether and -diphenyl sulphide, and of [1-, 2-, 3-, and 4-$^3H_1$]-dibenzofuran and -dibenzothiophen in anhydrous trifluoroacetic acid at 70·1°. The 2- and 4-positions of diphenyl ether are more reactive than those of diphenyl sulphide. The order of reactivity of the several positions of dibenzo-furan and -thiophen is $2 > 3 > 4 > 1$, the 2-position being more, and the other positions less reactive in the oxygen than in the sulphur compound. Positions *ortho* and *para* to the hetero-atom are less reactive in the cyclic than in the open-chain compounds, the difference being greater with the oxygen compounds, but positions *meta* to the hetero-atom are more reactive in the cyclic compounds.

WE have measured the rates of detritiation of [2- and 4-$^3H_1$]-diphenyl ether and -diphenyl sulphide, and of [1-, 2-, 3-, and 4-$^3H_1$]-dibenzofuran and -dibenzothiophen by trifluoroacetic acid at 70·1°, and the results are shown in the Table. We have also measured the rate of detritiation of [$^3H_1$]benzene under these conditions in order to derive rate factors, $f$, for the reactivities of the separate positions of the oxygen and sulphur compounds relative to the reactivity of a single position in benzene. These factors must be regarded as approximate because only 10% of reaction occurs with benzene in three months, but we have no reason to believe that the measured rate for benzene is in error by more than ±5%. (The reactivities of the separate positions of the oxygen and sulphur compounds relative to one another are, of course, unaffected by this uncertainty.) The factors are set out in the diagram below, some figures for toluene being included for comparison.

Rates of detritiation in trifluoroacetic acid at 70·1°.

| Aromatic compound | Posn. of $^3H$ | $10^6k$ (sec.$^{-1}$) | Aromatic compound | Posn. of $^3H$ | $10^6k$ (sec.$^{-1}$) | Aromatic compound | Posn. of $^3H$ | $10^6k$ (sec.$^{-1}$) |
|---|---|---|---|---|---|---|---|---|
| Diphenyl ether | 2 | 65·8 | Dibenzofuran | 1 | 1·28 | Dibenzothio-phen | 1 | 2·58 |
| | 4 | 293 | | 2 | 34·9 | | 2 | 17·4 |
| Diphenyl sulphide | 2 | 31·6 | | 3 | 2·97 | | 3 | 4·08 |
| | 4 | 93·4 | | 4 | 1·52 | | 4 | 3·44 |
| | | | | | | Benzene | 1 | 0·0095 |

The main features of the results are as follows:

(i) There is a large spread of rates in detritiation in trifluoroacetic acid, and thus probably also a large demand on polarizability effects in the aromatic systems concerned. For example, the rate factor, $f$, for the *para*-position of toluene, *viz.*, 450, is markedly greater than that in protodesilylation ($f = 20$) [2] or nitration ($f = 58$),[3] but less than that in molecular bromination ($f = 2420$) or chlorination ($f = 820$).[4] The values of $f$ in

[1] Part XIX, Baker, Eaborn, and Taylor, *J.*, 1961, 4927.
[2] Eaborn, *J.*, 1956, 4858.
[3] Cohn, Hughes, Jones, and Peeling, *Nature*, 1952, **169**, 291; cf. Knowles, Norman, and Radda, *J.*, 1960, 4885.
[4] Brown and Stock, *J. Amer. Chem. Soc.*, 1957, **79**, 1421, 5175.

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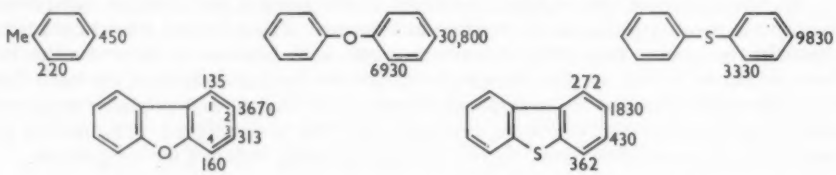
nitration for the 2- and 4-positions of diphenyl ether (117 and 234, respectively) and for the 1-, 2-, 3-, and 4-positions of dibenzofuran (47, 94, 94, and 0, respectively [6]) are all several times smaller than in detritiation.

(ii) The 2- and 4-positions of diphenyl ether are more reactive than the corresponding positions of diphenyl sulphide, in agreement with the smaller $+T$ effect of a sulphur than of an oxygen atom. The same result is found in protodesilylation,[7] but the differences are greater in that reaction; for example, the 4-position of diphenyl ether is 8 times more reactive than the 4-position of diphenyl sulphide in protodesilylation, but only 3 times in detritiation, in spite of the much greater spread of rates normally associated with detritiation.

The reactivity of the 4- relative to that of the 2-position of diphenyl ether ($\log f_4/\log f_2 = 1{\cdot}17$) agrees with that in nitration ($\log f_4/\log f_2 = 1{\cdot}14$),[5] but is much smaller than that in protodesilylation ($\log f_4/\log f_2 = 2{\cdot}07$),[7] and the difference between detritiation and protodesilylation in this respect is even more marked for diphenyl sulphide. The differences cannot reasonably be ascribed to steric influences at the 2-position, since primary steric effects are believed to be very small in hydrogen-exchange,[1] while steric interference from *ortho*-substituents normally results in acceleration of protodesilylation.[8]

The ratio of the reactivities of the 4- and 2-positions of diphenyl ether, *viz.*, 4·4, is somewhat greater than that for the 4- and 2-positions of anisole in dedeuteration, *viz.*, 2·4 in aqueous sulphuric acid at 25° [9] and 3·0 in sulphuric acid–acetic acid at 80°.[10]

(iii) Closure of the five-membered rings on going from diphenyl ether to dibenzofuran or from diphenyl sulphide to dibenzothiophen, is associated with a large reduction in reactivity of the positions *ortho* and *para* to the heteroatoms (cf. ref. 5), the reduction being much greater for those *ortho* than for those *para* to those atoms, and being greater for the oxygen than for the sulphur compounds. The effect is so large for positions *ortho* to the oxygen atom that the 4-position of dibenzofuran is less than half as reactive as the 4-position of dibenzothiophen, even though the corresponding 2-position of diphenyl ether is more than twice as reactive as that in diphenyl sulphide.




The reduction of reactivity on ring-closure is to be attributed mainly to the engagement of the lone-pair of the oxygen and sulphur atoms in giving aromatic character to the five-membered rings, the $+T$ effects of those atoms being made available to the 4- and 2-positions of the heterocyclic compounds only at the expense of this aromatic character.

Positions *meta* to the hetero-atoms are very greatly increased in reactivity by the ring closure. The values of $f$ for the 3-positions of diphenyl ether and sulphide are probably less than 1 (preliminary measurements indicate this to be the case for diphenyl ether), while the values for the 3-position of dibenzo-furan and -thiophen are 313 and 430, respectively, and for the 1-position are 135 and 272. The activation of the 1- and 3-positions is presumably to be attributed to the $+T$ effect of the substituted-phenyl group

[5] Dewar and Urch, *J.*, 1958, 3079.
[6] Dewar and Urch, *J.*, 1957, 345.
[7] Eaborn and Sperry, *J.*, 1961, 4921.
[8] Benkeser and Krysiak, *J. Amer. Chem. Soc.*, 1954, **76**, 6353; Benkeser, Hickner, Hoke, and Thomas, *ibid.*, 1958, **80**, 5289; Eaborn and Moore, *J.*, 1959, 3640; Eaborn, Lasocki, and Webster, *J.*, 1959, 3034.
[9] Satchell, *J.*, 1956, 3911.
[10] Lauer and Day, *J. Amer. Chem. Soc.*, 1955, **77**, 1904.

*ortho* and *para* to these positions, respectively (the 2- and 4-positions of biphenyl are activated 133 and 143 times, respectively, in detritiation in trifluoroacetic acid containing aqueous sulphuric acid,[11] and greater activation is to be expected when the two benzene rings are held co-planar [12]).

(iv) The 1-, 3-, and 4-positions are more reactive in dibenzothiophen than in dibenzofuran. In protodesilylation the 3-position of the oxygen compound is slightly the more reactive.[7] (In the latter reaction the reactivities of the 1-positions are influenced by steric effects.)

(v) In both dibenzofuran and dibenzothiophen the order of reactivity of the positions in detritiation is $2 > 3 > 4 > 1$.

(vi) The reactivity of the 2-position of dibenzothiophen represents 64% of the total reactivity of the 1-, 2-, 3-, and 4-positions. Thus in other electrophilic aromatic substitutions we should expect predominant but certainly not exclusive 2-substitution, though the substitution in the other positions might be too small to detect easily in a highly selective reaction such as molecular bromination. It is usually said that only 2-substitution occurs, but the experimental evidence available does not support this. All that can be said is that (except for the isolation of a little 4-derivative in acetylation [14]) only the 2-substituted product has been obtained pure from each reaction. From bromination the 2-bromo-compound is obtained in about 80% yield,[13] but other isomers could also be present. From nitration in acetic acid, Cullinane, Davies, and Davies isolated the 2-nitro-derivative in 40% yield along with an equal amount of dibenzothiophen 5-oxide,[13] but Gilman and Nobis could obtain the 2-nitro-derivative in only 28% yield.[14] Sulphonation is said to lead to 2-substitution, but no details are given.[15] Acetylation gives predominant 2-substitution, but Gilman and Nobis isolated the pure 2-acetyl derivative in only 41% yield,[14] while Burger, Wartman, and Lutz reported that a mixture is formed, and isolated only 25% of the 2-, along with a very small amount of the 4-acetyl derivative.[16]

(vii) In dibenzofuran the reactivity of the 2-position represents about 86% of the total reactivity of the 1-, 2-, 3-, and 4-positions in detritiation, and thus we should expect to find greater predominance of 2-substitution in other reactions than for dibenzothiophen. This should be particularly true for reactions of high selectivity, and only the 2-bromo-derivative has been isolated after molecular bromination, in about 80% yield.[17] Sulphonation is said to give exclusive 2-substitution,[18] but the facts are that 89% of a sodium salt was isolated, with no evidence that it was a single substance and, from this, pure 2-dibenzothiophensulphonyl chloride was obtained in 85% yield, so that at least 76% of 2-sulphonation must occur. In benzoylation the 2-derivative was isolated exclusively, but only in 40% yield.[19]

The results of mercuration and nitration are quite anomalous. Mercuration is said to give only 4-substitution;[20] although only 38% of the pure 4-derivative was isolated, even this amount is out of accord with the results in other substitutions. Possibly the acetoxymercuric group is attached first to the oxygen atom of dibenzofuran and then migrates to the adjacent 4-position, but anisole under comparable conditions gives mainly the *para*-derivative. (However, such attachment to oxygen might be less sterically hindered in the cyclic compound than in anisole.)

From nitration in acetic acid, up to 80% of 3-nitrodibenzofuran has been isolated,

[11] Eaborn and Taylor, *J.*, 1961, 1012.
[12] de la Mare and Ridd, "Aromatic Substitution. Nitration and Halogenation," Butterworths Scientific Publications, London, 1959, pp. 158—160.
[13] Cullinane, Davies, and Davies, *J.*, 1936, 1435.
[14] Gilman and Nobis, *J. Amer. Chem. Soc.*, 1949, **71**, 274.
[15] Courtot, *Compt. rend.*, 1934, **198**, 2260.
[16] Burger, Wartman, and Lutz, *J. Amer. Chem. Soc.*, 1938, **60**, 2628.
[17] Mayer and Krieger, *Ber.*, 1922, **55**, 1659.
[18] Gilman, Smith, and Oatfield, *J. Amer. Chem. Soc.*, 1934, **56**, 1412.
[19] Johnson, Willis, and Gilman, *J. Amer. Chem. Soc.*, 1954, **76**, 6407.
[20] Gilman and Young, *J. Amer. Chem. Soc.*, 1934, **56**, 1415.

XUM

along with a little of the 2- and possibly some of the 1-isomer.[21] Nitration in acetic anhydride is said to give 40% of 2- and of 3-, and 20% of 1-nitration.[6] These results seem to be inexplicable at present in terms of the concepts which serve to interpret reactivities of monosubstituted benzenes in common electrophilic substitutions. A suggestion[22] that the 3-nitration of dibenzofuran results from prior protonation of the oxygen atom is untenable.[7]

It must be stressed that (even when steric effects are ignored) change in the position of maximum reactivity of a complex aromatic compound from reaction to reaction is not in itself surprising, since the balance of polarization and polarizability factors differ from reagent to reagent. Towards a reagent of low electron demand a position of high electron density in the initial state may well be the point of maximum reactivity, whereas towards a reagent of high electron demand a position to which electromeric effects can operate most strongly is likely to be the most reactive. Compared with halogenation, deuteration, and sulphonation (see ref. 23), nitration has a low electron demand, and thus might bring about most substitution at a different position. However, not only is there no evidence of 3-nitration in dibenzothiophen (for which in detritiation, the 2- and 3-positions are less separated in reactivity than they are in dibenzofuran), but also in protodesilylation, which is a reaction of markedly lower electron demand than nitration, the 2-position of dibenzofuran is 8 times more reactive than the 3-position.[7]

It may be relevant that nitration of anisole by acetyl nitrate is also " anomalous " in that an abnormally high proportion of *ortho*-substitution occurs, and de la Mare and Ridd[24] (and later Norman and Radda[25]) have suggested that the nitrating species becomes initially attached to the oxygen atom, a rearrangement subsequently occurring. A similar initial step might be postulated for nitration of dibenzofuran (although an electrophile can be attached at oxygen only by destroying the aromatic character of the five-membered ring), but one is left with the difficulty of explaining why the rearrangement should give the 3-isomer.

Recent calculations of π-electron density in dibenzofuran and related heterocyclic compounds are said to " account fully for all observations on electrophilic substitution " in these compounds,[26] but for dibenzofuran it seems to have been assumed that the order of reactivity of the positions observed in nitration in acetic anhydride,[6] *viz.*, $2 = 3 > 1 > 4$, is general for all such substitutions, whereas it is clearly anomalous. It is evident that a theory which relates the reactivities of the several positions only to the π-electron densities in the initial aromatic molecule cannot hope to explain the different reactivity orders observed in different reactions.

## Experimental

*Preparation of Materials.*—Monotritiated compounds, having calculated activity (see ref. 27) of *ca.* 8 mc/g., were prepared by hydrolysing the appropriate arylmetal derivative with a 20—50% excess of tritiated water (100 mc/ml.) before an excess of ordinary water was added.[27] The arylmetal derivative was made in each case as described for preparation of trimethylsilyl derivatives.[7] Yields of [X-$^3H_1$] aromatic compounds were as follows:

(i) Diphenyl ether: 2-, 85%; 4-, 83% (m. p. in both cases, 28·0°). (ii) Diphenyl sulphide: 2, 86% (b. p. 145°/11 mm., $n_D^{20}$ 1·6346); 4-, 63% (b. p. 152°/18 mm., $n_D^{20}$ 1·6345). (iii)

[21] Cullinane, *J.*, 1930, 2267; Gilman and Swiss, *J. Amer. Chem. Soc.*, 1944, **66**, 1884.
[22] Hartough and Meisel, " Compounds with Condensed Thiophene Rings," Interscience Publ., Inc., New York, 1954, p. 12.
[23] Eaborn and Taylor, *J.*, 1960, 1480; Cerfontain, Kaandorp, and Sixma, *Rec. Trav. chim.*, 1960, **79**, 935.
[24] Ref. 12, p. 76.
[25] Norman and Radda, *Proc. Chem. Soc.*, 1960, 423.
[26] Brown and Coller, *Austral. J. Chem.*, 1959, **12**, 152.
[27] Eaborn and Taylor, *J.*, 1960, 3301.

Dibenzofuran: 1-, 48%; 2-, 78%; 3-, 66%; 4-, 90% (m. p. in each case, 86·0°). (iv) Dibenzothiophen: 1-, 60%; 2-, 88%; 3-, 70%; 4-, 92% (m. p. in each case, 99°).

*Rate Measurements.*—The general methods have been described.[11,27,28] Relative tritium activities were measured as galvanometer deflections by the Matsukawa and Eaborn's method.[29] All reactions were carried out in sealed tubes.

In calculation of " equilibrium " deflections [28] it was assumed that the following number of ring positions would be available for tritium at ten times the half-life of the exchange: [2-$^3H_1$]diphenyl ether and sulphide, 6; [4-$^3H_1$]diphenyl ether, [4-$^3H_1$]diphenyl sulphide, [2-$^3H_1$]dibenzo-furan and -thiophen, 2·5; [3-$^3H_1$]dibenzo-furan and -thiophen, 7; [1-$^3H_1$]- and [4-$^3H_1$]-dibenzo-furan and -thiophen, 8. Any errors introduced by the assumptions would be very small.

The following specimen run refers to [1-$^3H_1$]dibenzothiophen.

Five 1 ml. portions were transferred to tubes from a solution of the tritiated compound (0·0149 g.) in trifluoroacetic acid (7·8366 g.), and the residue weighed 0·429 g. There was thus 0·0028 g. of the [1-$^3H_1$]dibenzothiophen in each tube, and separate measurement showed that this amount, when dissolved in 10 ml. of toluene, gave, under our standard conditions of measurement, a deflection of 76·2 mm. On the assumption that one position of trifluoroacetic acid and eight of dibenzothiophen are equally available for tritium, at ten times the half-life of the exchange 0·9% of the tritium will be in the aromatic compound, and 8·8 g. of toluene extract will give a deflection, $D_\infty$, of 0·7 mm.

In the following Table, $D_t$ is the deflection for 8·8 g. of toluene extract at a time, $t$, measured from the time of removal of the first tube from the bath. If $D_0$ is the deflection resulting from this first sample, the *pseudo*-first-order rate constant, $k$, is given by

$$kt = 2{\cdot}303 \log [(D_0 - D_\infty)/(D_t - D_\infty)]$$

| | | | | | |
|---|---|---|---|---|---|
| $t$ (hr.) | 0·0 | 30·2 | 70·7 | 95·4 | 142·85 |
| $D_t$ (mm.) | 55·2 | 41·8 | 28·5 | 22·6 | 14·6 |
| $10^7k$ (sec.$^{-1}$) | — | 25·6 | 26·0 | 26·0 | 25·9 |

Mean rate constants, usually obtained graphically, could be duplicated to within $\pm 1{\cdot}5\%$.

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THE UNIVERSITY, LEICESTER. [*Received, June 12th*, 1961.]

[28] Eaborn and Taylor, *J.*, 1961, 247.
[29] Matsukawa and Eaborn, *Research* (Correspondence), 1956, **9**, S37; Eaborn, Matsukawa, and Taylor, *Rev. Sci. Instr.*, 1957, **28**, 725.

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## 1006. *Aromatic Reactivity. Part XXI.*[1] *Effects of Strongly Deactivating Substituents in Protodetriethylgermylation.*

By C. Eaborn and K. C. Pande.

We have measured the rates of cleavage of some aryltriethylgermanes, $X{\cdot}C_6H_4{\cdot}GeEt_3$, in a mixture of acetic acid and aqueous sulphuric acid at 50·0°. The substituents, X, include halogen atoms, and carboxyl-, trifluoromethyl-, trimethylammonio-, and nitro-groups, all in *meta*- as well as *para*-positions. For some of the substituents the results provide the first quantitative measure of their effects in an electrophilic aromatic substitution.

The nitro-, trimethylammonio-, and trifluoromethyl groups deactivate little more from the *meta*- than from the *para*-position, in contrast with their behaviour in nitration. In the case of groups for which the necessary substituent constants are available, the results fit the Yukawa–Tsuno equation precisely.

We recently described the effects of some nuclear substituents on the rates of cleavage of triethylphenylgermanes by aqueous-methanolic perchloric acid.[2] The most deactivating substituent we could conveniently study in that medium was *m*-chloro, and to obtain information on the effects of groups which withdraw electrons more strongly we have measured the rates of cleavage of some substituted triethylphenylgermanes, $X{\cdot}C_6H_4{\cdot}GeEt_3$, in a mixture of acetic acid (containing 0·80% of water) and aqueous sulphuric acid at 50·0°, a medium previously used for cleavage of aryltrimethylsilanes.[3]

The results are shown in Table 1, which lists the concentration of sulphuric acid taken (1 volume of which was mixed with 2 volumes of acetic acid), the observed first-order rate constants, $k$, and the rates, $k_{rel.}$, relative to that of the unsubstituted compound, $C_6H_5{\cdot}GeEt_3$. The values of $k_{rel.}$ provide the first accurate measure of the effects of some of the substituents in an electrophilic aromatic substitution.

Table 1.

Cleavage of $X{\cdot}C_6H_4{\cdot}GeEt_3$ compounds in $CH_3{\cdot}CO_2H$–$H_2O$–$H_2SO_4$ at 50·0°.

| X | $H_2SO_4$ (M) | $10^3k$ (min.$^{-1}$) | $k_{rel.}$ | X | $H_2SO_4$ (M) | $10^3k$ (min.$^{-1}$) | $k_{rel.}$ |
|---|---|---|---|---|---|---|---|
| *p*-OMe | 0·295 | 55·4 | 392 | *m*-Br | 9·65 | 13·7 | 0·019 |
| *o*-OMe | 0·295 | 26·0 | — | *m*-Cl | 9·65 | 13·5 | 0·0191 |
| | 1·42 | 191 | 187·5 | | 11·67 | 76·5 | — |
| *p*-Me | 1·42 | 12·7 | — | *m*-$CO_2H$ | 11·67 | 71·0 | 0·0177 |
| | 3·62 | 79·4 | 12·4 | *m*-$CF_3$ | 11·67 | 21·7 | $5{\cdot}4 \times 10^{-3}$ |
| *p*-Ph | 3·62 | 15·55 | — | | 13·85 | 73·75 | — |
| | 5·55 | 69·3 | 2·43 | *p*-$CF_3$ | 11·67 | 9·84 | $2{\cdot}46 \times 10^{-3}$ |
| *m*-Me | 5·55 | 50·8 | 1·78 | | 13·85 | 36·1 | $2{\cdot}55 \times 10^{-3}$ |
| H | 5·55 | 28·5 | 1 | *p*-$CO_2H$ | 11·67 | 20·65 | $5{\cdot}2 \times 10^{-3}$ |
| | 6·45 | 63·1 | 1 | | 14·20 | 123·6 | — |
| *m*-OMe | 6·45 | 32·1 | 0·51 | *m*-$NMe_3^+$ | 14·20 | 30·2 | $12{\cdot}6 \times 10^{-4}$ |
| *p*-Cl | 6·45 | 10·6 | 0·168 | *p*-$NMe_3^+$ | 14·20 | 25·3 | $10{\cdot}6 \times 10^{-4}$ |
| *p*-Br | 6·45 | 8·40 | 0·133 | *m*-$NO_2$ | 14·20 | 19·1 | $8{\cdot}0 \times 10^{-4}$ |
| | 9·65 | 94·3 | — | *p*-$NO_2$ | 14·20 | 9·00 | $3{\cdot}76 \times 10^{-4}$ |
| *m*-F | 9·65 | 22·4 | 0·032 | | | | |

The main features, and some comments, are as follows. (*a*) For substituents examined in both media (*viz.*, *p*-OMe, *o*-OMe, *p*-Me, *p*-Ph, *m*-Me, *m*-OMe, *p*-Cl, *p*-Br, and *p*-I), a plot of log $k_{rel.}$ for cleavages in $CH_3{\cdot}CO_2H$–$H_2O$–$H_2SO_4$ against log $k'_{rel.}$ for cleavages in MeOH–$H_2O$–$HClO_4$ is precisely linear (log $k_{rel.}$ = 0·95 log $k'_{rel.}$). The slope of the line coincides, within experimental error, with that of the analogous plot[3] for aryltrimethylsilanes.

As has been pointed out before,[2,3] the composition of both types of medium varies

[1] Part XX, Baker and Eaborn, preceding paper.
[2] Eaborn and Pande, *J.*, 1961, 297.
[3] Deans and Eaborn, *J.*, 1959, 2299.

somewhat as the concentration of the added acid is changed, and values of $k_{rel.}$ are not necessarily exactly those which would be obtained if all the compounds were examined at one acid concentration, but the precision of the linear free-energy relation just noted confirms our view that no serious error in substituent effects is introduced by neglect of the medium change. It also indicates that the polar properties of the substituents concerned are not specifically affected by the change from $MeOH–H_2O–HClO_4$ to $CH_3·CO_2H–H_2O–H_2SO_4$.

(*b*) Where analogous compounds, $X·C_6H_4·GeEt_3$ and $X·C_6H_4·SiMe_3$, have been studied in $CH_3·CO_2H–H_2O–H_2SO_4$ (*viz.*, X = *o*-, *m*-, and *p*-OMe, *p*-Me, *p*-Ph, *m*- and *p*-Cl, *p*-$CO_2H$, *p*-$NMe_3^+$, and *p*-$NO_2$) a linear free-energy relation, $\log k_{rel.}^{Ge} = 0{\cdot}86 \log k_{rel.}^{Si}$, applies.

(*c*) As in protodetrimethylsilylation,[3] the nitro-group deactivates *meta*- and *para*-positions more than does the trimethylammonio-group. This means that withdrawal of electrons from the *meta*- and *para*-positions is stronger with the nitro-group, particularly when it is remembered that the rate of reaction of a positively charged ammonium compound with a positively charged electrophile is lowered by external electrostatic effects (which influence the entropy term and not the activation energy term in the rate equation [3,4]) below that which result from internally transmitted polar effects.[3] The effect of the nitro-group on the basicity of amines [5] and on the rate of *meta*-bromination of nitropolyalkylbenzenes is not much altered when steric effects force the group from the plane of the ring, and thus decrease the conjugation with the ring, and this is consistent with electron-withdrawal by the nitro-group's being almost wholly inductive, and originating in the positive charge on the nitrogen atom in the dipolar-ion group (cf. ref. 7). But if this were so, we should expect deactivation by the nitro-group, in which the effect of the positive charge on the nitrogen atom is partly neutralized by the negative charge distributed between the oxygen atoms, to be markedly smaller than that by the trimethylammonio-group, which has a unit positive charge on nitrogen; we conclude (as de la Mare and Ridd have done after considering the relative effects of a nitro-group on the *ortho*- and *para*-positions [7]) that the $-M$ effect of the nitro-group must also be important. The contribution of the $-M$ effect to deactivation of the *meta*-position presumably comes from secondary relay to the reaction centre of part of the excess of positive charge induced on positions *ortho* and *para* to it.

(*d*) As would be expected from their powerful *meta*-directing effects in nitration, the strongly electron-withdrawing nitro-, trimethylammonio-, and trifluoromethyl-groups deactivate the *para*- more than the *meta*-position,* but the most striking feature is that for each group the difference between its effect on the *meta*- and on the *para*-position is small. The smallness of the ratios $k_{rel.}^m/k_{rel.}^p$ for the three groups (*viz.*, $NO_2$, 2·1; $CF_3$, 2·2; $NMe_3^+$, 1·2) contrasts sharply with the $\frac{1}{2}m/p$ product ratio of 155 in nitration of nitrobenzene,[7] and the 100% *meta*-orientation in nitration of the phenyltrimethylammonium ion and of trifluoromethylbenzene.[8] Similarly small $k_{rel.}^m/k_{rel.}^p$ ratios for these substituents were found for solvolysis of substituted αα-dimethylbenzyl chlorides in 90% aqueous acetone at 25° (*viz.*, $NO_2$, 3·4; $CF_3$, 2·7; $NMe_3^+$, 1·7), and were held to be consistent with the groups' acting predominantly through inductive effects,[9,10] but the sharp discordance

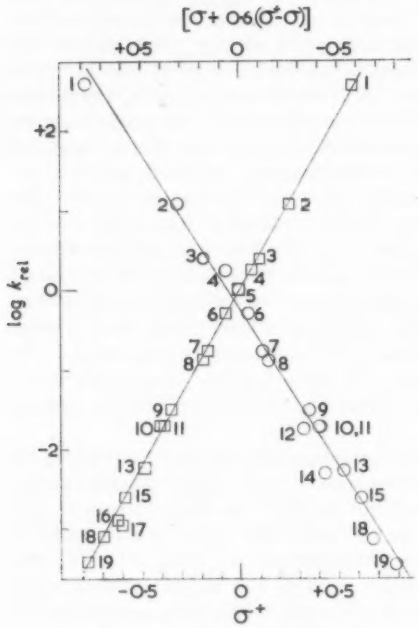
* We find that in aqueous sulphuric acid, however, *m*- reacts more slowly than *p*-trimethylammoniophenyltriethylgermane. The effects of charged groups are known to be particularly sensitive to medium changes, but such a reversal of the relative deactivating influence of *m*- and *p*-trimethylammonio-substituents means their behaviour is more difficult to interpret than has been appreciated before.

[4] Frost and Pearson, "Kinetics and Mechanism," John Wiley and Sons Inc., New York, 2nd edn., 1961, pp. 142—145.
[5] Wepster, *Rec. Trav. chim.*, 1956, **75**, 1473.
[6] Illuminati, *Nature*, 1957, **179**, 780.
[7] de la Mare and Ridd, "Aromatic Substitution. Nitration and Halogenation," Butterworths Scientific Publications, London, 1959, pp. 82—83.
[8] Ref. 7, p. 8.
[9] Okamoto, Inukai, and Brown, *J. Amer. Chem. Soc.*, 1958, **80**, 4969.
[10] Okamoto and Brown, *J. Amer. Chem. Soc.*, 1958, **80**, 4976.

with the effects of the substituents in nitration remains unexplained; the picture is further complicated by indications from indirect measurements, that the nitro-group may deactivate the *meta*- more than the *para*-position towards molecular chlorination.[11]

The value of $k^m_{rel.}/k^p_{rel.}$ for the carboxyl group in the cleavage (*viz.*, 3·4) cannot be regarded as inconsistent with the $\frac{1}{2}m/p$ product ratio in nitration of benzoic acid (*viz.*, 31),[7] in view of the greater spread of rates usual in nitration (*e.g.*, the deactivating effect of the *m*-chloro-substituent is 20 times greater in nitration [12] than in the cleavage). The carboxyl group deactivates less than the trifluoromethyl group in both *meta*- and *para*-positions, and in the *meta*-position has an effect very similar to that of the chloro-substituent.

(*e*) Deactivation by *meta*-halogen is in the order Cl = Br > F. The smaller effect of a *m*-fluoro-compound compared with that of a *m*-chloro- or *m*-bromo-substituent has been noted previously in detritiation [13] (for which, however, only approximate results




Plot of log $k_{rel.}$ for cleavage of $X{\cdot}C_6H_4{\cdot}GeEt_3$ compounds against $\sigma^+$ (circles) or $[\sigma + 0{\cdot}6(\sigma^+ - \sigma)]$ (squares).

1, *p*-OMe. 2, *p*-Me. 3, *p*-Ph. 4, *m*-Me. 5, H. 6, *m*-OMe. 7, *p*-Cl. 8, *p*-Br. 9, *m*-F. 10, *m*-Br. 11, *m*-Cl. 12, *m*-$CO_2H$. 13, *m*-$CF_3$. 14, *p*-$CO_2H$. 15, *p*-$CF_3$. 16, *m*-$NMe_3^+$. 17, *p*-$NMe_3^+$. 18, *m*-$NO_2$. 19, *p*-$NO_2$.

were obtained), and in molecular bromination of substituted polymethylbenzenes in nitromethane,[14] and it indicates that the $+T$ effect of fluorine is able to influence the *meta*-reaction site, presumably by secondary relay from positions *ortho* to this site.[15]

(*f*) A plot of log $k_{rel.}$ against the $\sigma^+$-constants [16] for the various substituents approximates to a straight line (see Figure), but from any line drawn through the origin there are real deviations for some points, including those for *p*-phenyl and *p*-chloro-substituents, whose behaviour is known not to be adequately interpretable in terms of their $\sigma^+$-constants.[17] The biggest deviation from the line drawn in the Figure involves

[11] Ref. 7, p. 146.
[12] Ref. 7, p. 85.
[13] Eaborn and Taylor, *J.*, 1961, 2388.
[14] Illuminati and Marino, *J. Amer. Chem. Soc.*, 1956, **78**, 4975.
[15] Brown, Okamoto, and Ham, *J. Amer. Chem. Soc.*, 1957, **79**, 1906.
[16] Brown and Okamoto, *J. Amer. Chem. Soc.*, 1958, **80**, 4979.
[17] Eaborn, *J.*, 1956, 4858; Eaborn and Taylor, *J.*, 1961, 1012; Kohnstam, *J.*, 1960, 2066.

the *p*-carboxyl group, and, as in cleavage of trimethylphenylsilanes,[3] a point nearer the line is obtained if the $\sigma^+$-constant for the *p*-methoxycarbonyl group ($CO_2Me$) is used.* Much bigger deviations occur with *m*- and *p*-trimethylammonio-groups, but we have omitted these from the plot because of the known difficulty of applying substituent constants to charged groups.

Application of the Yukawa–Tsuno equation,[19] $\log k_{rel.} = \rho[\sigma + r(\sigma^+ - \sigma)]$, leads to an excellent straight line (the values of $\rho$ and $r$ being 4·4 and 0·6, respectively), with all the substituents for which approriate $\sigma$- and $\sigma^+$-constants [16] are available. (It must be stressed that only $\sigma$-constants derived from ionization of substituted benzoic acids [20] must be used, not those deduced indirectly.) It is particularly significant that the results for the *meta*- and *para*-nitro- and -trifluoromethyl substituents, which cannot be reconciled with results in nitration, agree precisely with an equation which applies [19] to a wide range of electrophilic aromatic substitutions and side-chain reactions; it may mean that the results in nitration are not typical of those in electrophilic aromatic substitutions as a whole. (The same observation could have been based, of course, on the poorer but still reasonable fit of the points for the nitro and trifluoromethyl substituents to the log $k_{rel.}$—$\sigma^+$ plot.) It is noteworthy, too, that even points for the *m*- and *p*-trimethylammonio-substituents are reasonably close to the line; this may be coincidental, but if the Yukawa–Tsuno equation proved capable of interpretating the effects of these groups, even semi-quantitatively, in a range of reactions it would be a considerable achievement.

## Experimental

*Materials.*—The preparations of the organogermanium compounds have been described,[21] except for those of the trimethylammonio-compounds which were made as follows.

A mixture of *m*- or *p*-dimethylaminophenyltriethylgermane and methyl iodide was kept at 40° for 0·5 hr., and the resulting *methiodide* recrystallized from ethanol–acetone to give the *m*-, m. p. 148—150° (with bubbling) (Found: C, 42·9; H, 6·9; N, 3·4. $C_{15}H_{28}GeIN$ requires C, 42·7; H, 6·7; N, 3·3%), or *p*-isomer, m. p. 203—205° (with bubbling) (Found: C, 42·7; H, 6·7; N, 3·3%). The iodides were hydrolysed to the hydroxides (which were used in the rate studies) by boiling them with an aqueous suspension of silver oxide, and after filtration water was evaporated at low pressure to leave a material which was taken up in methanol. The solution was filtered, and the residue was dissolved in anhydrous ethanol. Addition of ether gave the crystalline *hydroxides* [Found: N, 4·7 (*m*-isomer) and 4·5 (*p*-isomer). $C_{15}H_{29}GeNO$ requires N, 4·5%].

The acetic acid, purified as previously described,[3] contained 0·80% of water.

Table 2.

| X | $10^3$ Concn. (M) | λ (mμ) | X | $10^3$ Concn. (M) | λ (mμ) |
|---|---|---|---|---|---|
| *p*-OMe | 1·7 | 283 | *m*-Cl | 9 | 279 |
| *o*-OMe | 1·2 | 283, 286 | *m*-Br | 8·5 | 281 |
| *p*-Me | 10 | 274, 275 | *m*-$CO_2H$ | 0·7 | 289, 290 |
| *p*-Ph | 1 | 292 | *p*-$CO_2H$ | 0·7 | 285, 286 |
| H | 9 | 267, 268 | *m*-$CF_3$ | 6 | 274 |
| *m*-OMe | 1·7 | 286 | *p*-$CF_3$ | 6 | 274 |
| *p*-Cl | 8 | 278 | *m*-$NMe_3^+OH^-$ | 10 | 269 |
| *p*-Br | 8 | 276 | *p*-$NMe_3^+OH^-$ | 5 | 269 |
| *m*-F | 8 | 277 | *m*-$NO_2$ | 6·5 | 370 |
| | | | *p*-$NO_2$ | 9 | 370 |

*Rate Measurements.*—Techniques were as previously described.[3] A solution (2 vol., of concentration shown in Table 2) of the organogermane in acetic acid was mixed with aqueous

* Deans and Eaborn suggested that the $\sigma^+$-constants for the carboxyl groups might be in error, but there are now indications [18] that there is interaction between the groups and the cleavage medium possibly involving protonation of the group. This is being studied.

[18] Greasley, unpublished work.
[19] Yukawa and Tsuno, *Bull. Chem. Soc. Japan*, 1959, **32**, 971.
[20] McDaniel and Brown, *J. Org. Chem.*, 1958, **23**, 420.
[21] Eaborn and Pande, *J.*, 1960, 3200; Eaborn, Leyshon, and Pande, *J.*, 1960, 3423.

sulphuric acid (1 vol.) of the strength shown in Table 1. Optical densities at the wavelengths, λ, noted in Table 2 were recorded at suitable times. The temperature of the cells was controlled at 50·0° ± 0·03°.

Rate constants from duplicate runs normally agreed within 3%, usually within 1·5%. For the *m*-nitro- and *m*-bromo-compounds, however, the optical density changes available were too small for accuracy, and in these cases the rate constants could be in error by ±10%.

Measurements of the optical densities at 269 mμ of solutions of the *m*- and *p*-triethylgermylphenyltrimethylammonium hydroxides in 7·6M-aqueous sulphuric acid (*ca.* 0·01 g. in 10 ml.) at 50·0° led to first-order rate constants of 0·064 and 0·084 min.$^{-1}$, respectively.

This work was supported in part by the U.S. Department of Army through its European Office. We thank the Royal Society for the loan of apparatus, and the General Electric Co., Ltd., for a gift of germanium dioxide.

THE UNIVERSITY, LEICESTER. [*Received, July 11th,* 1961.]

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## 1007. *The Rôle of Supports in Catalytic Hydrogenation. Part II.* Further Effects of Various Oxide Supports on the Activity of Platinum.*

By E. B. MAXTED and J. S. ELKINS.

The relative activities of hydrogenation catalysts consisting of a constant amount of platinum supported on a varied amount of zirconia, alumina, or chromium sesquioxide have been determined, over a wide range of platinum-to-support ratios, for the liquid-phase hydrogenation of cyclohexene and ethyl crotonate. Values for the mean pore radii of these supports have been calculated from the respective specific surface areas and from micropore volume measurements, by using the B.E.T. nitrogen-adsorption and the mercury-penetration method. The difference in activity for the hydrogenation of cyclohexene and of ethyl crotonate is dependent on the mean pore radius, in addition to the nature of the support. This seems to imply that the pore factor is important, especially if the supported catalyst is used for the hydrogenation of a large molecule. The poisoning method described by Maxted, Moon, and Overgage [1] has been used to estimate the relative surface areas of the supported platinum. Evidence, which cannot be accounted for by surface extension alone, is provided for the specific effects of supports.

THE present work continues that described in Part I.*

*Experimental.*—The catalysts used were prepared by allowing a known quantity of the various oxides to remain for 30 min. in contact with a dilute aqueous solution of chloroplatinic acid sufficient, after reduction, to give 6·25 mg. of metallic platinum. The suspensions were then stirred mechanically and heated to their boiling point and an excess of 40% formaldehyde solution was added. After 15 min. the supported platinum was centrifuged off, washed, and dried at 50°.

The hydrogenation tests were carried out at 20° and at atmospheric pressure, in alcoholic solution in a mechanically driven hydrogenation pipette, the charge of catalyst consisting in each case of 6·25 mg. of platinum carried on a varied amount of each of the supports. The system hydrogenated contained 1 c.c. of cyclohexene (or 1·5 c.c. of ethyl crotonate) dissolved in sufficient ethyl alcohol to give a total volume of 10 c.c. It was not found necessary to purify the cyclohexene; but it was found that the hydrogenation rate of ethyl crotonate was raised by a maximum of 5% by shaking this twice with reduced nickel supported on kieselguhr. The course of the hydrogenation was approximately of zero order; and the hydrogenation rate in c.c. per minute, reduced to N.T.P., was taken as a measure of the activity of the catalyst used.

The poisoning experiments were carried out in a similar way to the activity measurements

* Part I, *J.*, 1960, 1995.

[1] Maxted, Moon, and Overgage, *Discuss. Faraday Soc.*, 1950, **8**, 135.

for the hydrogenation of cyclohexene, except that the system contained a known amount of the poison, ethyl sulphide. The hydrogenation was of almost zero order during the first few minutes; and the rate over this period was taken as a measure of the poisoned activity.

The B.E.T. surface areas were determined from adsorption isotherms with purified nitrogen at −183°, the cross-sectional area of a nitrogen molecule being taken as 15·4 Å$^2$. Micropore volumes were calculated from helium density measurements, on spectroscopically pure helium, and from mercury density measurements, which were made [2] at a pressure of 1000 mm.

*Results and Discussion.*—Plots of the catalytic activities against increasing areas of the various supports, carrying a constant amount of platinum, are given in Fig. 1 for the hydrogenation of cyclohexene, and in Fig. 2 for the corresponding hydrogenation of ethyl crotonate, the relative activity of 6·25 mg. of unsupported platinum being shown by a single point at zero on the support-area axis. It will be seen that zirconia and the specially fine-grained specimen of alumina-I (of a size passing completely through a 200-mesh sieve) were by far the most active supports tested. The activity was also dependent to a large degree on the particle size of each of the supports, as well as on their chemical nature. Thus, a large-grained alumina (alumina-II; 100—200 mesh) gave a far less active catalyst than alumina-I, with, however, the peak activity in approximately the same position along the support-area axis. It will also be seen that, as would be expected, the position of the peak activity along the horizontal axis was independent of the substance hydrogenated.

The curves for zirconia and chromia rise relatively rapidly, and those for alumina much less steeply, to a peak point, after which the fall in activity is slower than the initial rise. Zirconia is the most active support for both reactions and raises the activity to nearly 22 times its unsupported value for the hydrogenation of cyclohexene, and to about 16 times this figure for the hydrogenation of ethyl crotonate.

From the ratio of platinum to support at the peak activity, it can be shown [3] that the platinum occupies a very small fraction (less than 4%) of the carrier surface. The absolute surface area of the platinum was not known; but an approximate value of the percentage coverage can be obtained if it is assumed that the platinum is dispersed to its fullest extent, *i.e.*, as a monatomic layer. The real coverage will be considerably less than this approximate value, since it is known that the platinum is present on the surface of the carrier as crystallites and would accordingly occupy a much smaller fraction of the surface than if it were present as a monolayer.[4]

The calculated weight of support necessary to accommodate a monolayer of 6·25 mg. of platinum is compared in Table 1 with that at the peak activity. The ratio of the calculated weight of support to that at the peak activity gives the coverage, or the ratio of the area of a monolayer of platinum to that of the support at the peak activity.

TABLE 1.

| Support | Calc. wt. of support reqd. for monolayer dispersion of platinum (g.) | Wt. of support at peak activity (g.) | Calc. coverage (%) |
|---|---|---|---|
| $Al_2O_3$-I | 0·0072 | 0·65 | 1·16 |
| $Cr_2O_3$ | 0·0245 | 0·75 | 3·23 |
| $Al_2O_3$-II | 0·0753 | 6·0 | 1·25 |
| $ZrO_2$ | 0·0993 | 2·25 | 4·41 |

The initial rise in the activity curves is probably due to two causes. If the amount of the support is small, the whole of the chloroplatinic acid may not be adsorbed from the solution during the preparation of the catalyst, so that, on reduction, some of the platinum

[2] Juhola and Wiig, *J. Amer. Chem. Soc.*, 1949, **71**, 2078.
[3] W. B. Innes, "Catalysis," ed. P. M. Emmett, Reinhold Publ. Corp., New York, 1954, Vol. I, p. 258.
[4] Maxted and Akhtar, *J.*, 1960, 405, 1995.

is reduced to the metallic state in the solution rather than on the support. Alternatively, complete adsorption of the chloroplatinic acid by small amounts of carrier might lead to large crystallites of platinum, as a result of the close proximity of the adsorption sites of $PtCl_6^{2-}$ ions on the carrier surface, before reduction. As the amount of support is increased, with a constant weight of platinum, either more platinum is formed on the support, or that which is formed consists of smaller crystallites. It was possible to distinguish unsupported from supported platinum by the dense black colour of the former, and by the difficulty in its separation by centrifugation. Even with large amounts (up to 4 g.) of alumina-II (100—200 mesh), some unsupported platinum was formed.

The reasons for the fall in activity may also be of two sorts: namely, (i) the platinum crystallites may be so small that the two-point adsorption of the unsaturated molecule on a single crystallite of the platinum becomes impossible, or (ii) an excess of bare support may cover areas of the supported metal and in this way hinder the free diffusion of reactant molecules to, and of molecules of product from, the active surface. If (i) is correct, the specific surface area of the platinum should continue to increase as the amount of the support is increased; whereas, if (ii) is correct, the most active catalysts should have a maximum available surface of platinum.

Plots of the poisoned activity, $k_c$, for each supported catalyst against the total poison present are linear for small quantities of poison and may be represented [1] by the equation $k_c = k_0(1 - \alpha c)$, in which $k_c$ is the activity in the presence of $c$ moles of poison, $k_0$ is the unpoisoned activity, and $\alpha$ is the poisoning coefficient, which is inversely proportional to the surface area. If $c_0$ is the value of $c$ when $k_c = 0$, then $\alpha = 1/c_0$, and $c_0$, the intercept of the extrapolated linear plot with the poison concentration axis, is proportional to the surface area of the platinum.

There is no direct dependence of the activity of the peak amount of each support (italicised in Table 2), on the surface area of the supported platinum, represented by the values of $c_0$ in Table 2, since the platinum supported by zirconia has a smaller relative

TABLE 2.

| Support | Amount (g.) | $k_0$ (cyclohexene) (c.c. of $H_2$ absorbed per min.) | $c_0$ ($10^{-7}$ mole) | $k_0\alpha$ ($10^7$ c.c. per min. per mole) |
|---|---|---|---|---|
| $ZrO_2$ | *2·25* | 45·5 | 9·5 | 4·8 |
| $Al_2O_3$-I | 0·05 | 35·0 | 12·2 | 2·9 |
| | 0·30 | 42·0 | 13·4 | 3·1 |
| | *0·60* | 44·8 | 14·0 | 3·2 |
| | 0·75 | 41·7 | 13·2 | 3·2 |
| | 1·00 | 39·5 | 12·8 | 3·0 |
| $Cr_2O_3$ | *0·75* | 38·7 | 12·5 | 3·1 |
| $Al_2O_3$-II | *6·00* | 18·8 | 8·9 | 2·1 |

surface than that supported by alumina-I, although their activities are almost the same. If the activity of these catalysts were dependent only on the surface area of the platinum, the respective values of $k_0\alpha$ would be the same for each support. Actually they are different, which indicates that the effect of each support is specific, the specificity being most marked in the case of zirconia.

The relative surface area of platinum supported by different amounts of alumina-I does not continue to increase as the amount of support is increased beyond that required for maximum activity, but falls as the activity decreases. Accordingly factor (ii), put forward above for the fall in activity, outweighs any effects due to (i).

When a metal is deposited on a porous support, some of the active surface becomes unavailable for catalysis by being contained in pores. Even if the mean pore radius is large compared with the size of the reacting molecules, the activity may, for the following reasons, be decreased by this deposition of platinum in the pores. The growth of platinum crystallites may occur across the mouth of a pore, in such a way as to block the entry of

molecules of reactant to the platinum which has been deposited with the pore. Further, the pore radius may be substantially reduced by the thickness of the metal layer on the internal surface of the pore; and, according to the size and shape of the pore and of the potentially adsorbable molecule, diffusion of reactant or resulting molecules to or from the active surface will be inhibited to a greater or lesser degree.

The use of a carrier with small pores to support the platinum would accordingly be expected to lead to a decreased activity, compared with that of the same amount of platinum of equal surface area deposited on a non-porous carrier, owing to the unavailability to a large molecule of part of the internal catalyst surface, the extent of the decrease in activity becoming greater the smaller the mean pore radius and the larger the unsaturated

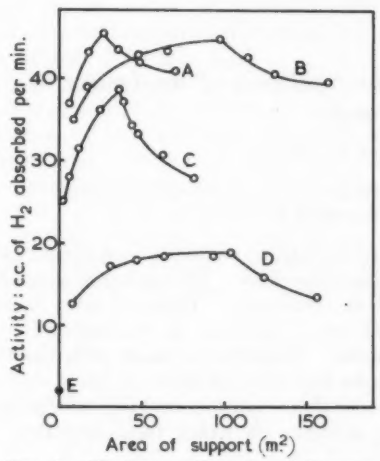


FIG. 1. Hydrogenation of cyclohexene.

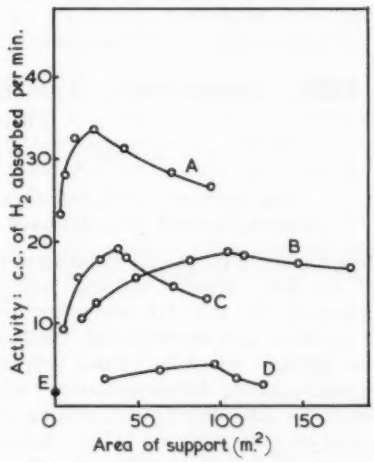


FIG. 2. Hydrogenation of ethyl crotonate.

Key (for both Figs.): A, $ZrO_2$; B, $Al_2O_3$-I; C, $Cr_2O_3$; D, $Al_2O_3$-II; E, unsupported Pt.

molecule hydrogenated. For these reasons, the activity of a given weight of platinum on a porous carrier, when this is used for the hydrogenation of unsaturated molecules of different molecular sizes, would be expected to differ owing to this difference in the molecular size, as well as to any difference due to the chemical nature of the molecule hydrogenated. Further, this difference would depend to some degree on the mean pore radius of the carrier. The difference in the activity of each of the supported catalysts used for the hydrogenation of cyclohexene and of ethyl crotonate has been compared in Table 3 with the mean pore radius of the respective supports.

TABLE 3.

| Support | $Al_2O_3$-I | $Cr_2O_3$ | $Al_2O_3$-II | $ZrO_2$ |
|---|---|---|---|---|
| Mean pore radius (Å) | 21 | 136 | 224 | 382 |
| Activity difference for cyclohexene and ethyl crotonate at the peak ratio (c.c. per min.) | 26·0 | 20·0 | 13·8 | 11·8 |

It will be seen from Fig. 1 that zirconia and alumina-I have almost the same activity at their peak ratios for the hydrogenation of cyclohexene, whereas, for the corresponding hydrogenation of ethyl crotonate, there is a wide difference in their activities. It is evident that the two supports are equally active for the hydrogenation of the smaller molecule, and that the fine pore structure of alumina-I is the cause of its relatively lower activity, compared with that of zirconia, for the hydrogenation of the larger molecule of

ethyl crotonate. The evidence for the influence of the pore size of the carrier on the activity of the platinum is confirmed by the values in Table 3. The reduction in the active surface available for catalysis, represented by the figures in the second column, corresponds with the mean pore radius of the support. Accordingly, the greatest difference in activity occurs in the case of alumina-I, which has the smallest pore size, whereas the smallest difference occurs for a zirconia-supported catalyst, which has the largest pore size. Chromium sesquioxide and alumina-II have activity differences which lie between those of alumina-I and zirconia and, for each of these carriers, the activity difference is less for the support with the greater mean pore radius.

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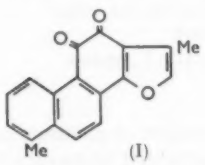
## 1008. *Tanshinones. Part I. The Synthesis of an Isomer of Tanshinone-I.*

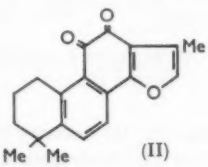
By T. J. KING and G. READ.

The synthesis is described of 4,5-dihydro-3,8-dimethyl-4,5-dioxophenanthro[4,3-*b*]furan (IV), an isomer of tanshinone-I (I).

IN 1930 Nakao [1] reported the isolation of three red crystalline pigments from the purgative drug " tan-shin " which is the dried roots of *Salvia miltorrhiza*. The pigments were called tanshinone-I, -II, and -III, and were identified as *o*-quinones. Takiura [2] later repeated their isolation and showed that tanshinone-III was a mixture of tanshinone-II with another pigment which he termed cryptotanshinone. Degradative work with the three pigments, including dehydrogenation [3] which shows that they all have the same skeleton, has led to the following structures being proposed for them, tanshinone-I (I), tanshinone-II (II), and cryptotanshinone (III). Most of the evidence on which these structures are



(I)



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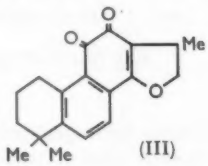

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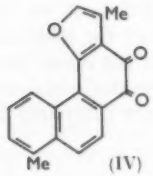
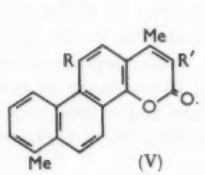
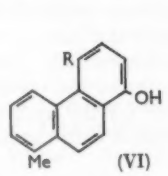


(IV)



(V)



(VI)

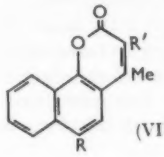
based has been obtained by Takiura [4] or by von Wessely and his co-workers [4] and has been admirably summarised.[5] The possible biogenetic relationship of all these pigments to the diterpenes was first emphasised by Todd.[6]

[1] Nakao, *Bull. Shanghai Sci. Inst.*, 1930, V; Nakao and Fukushima, *J. Pharm. Soc. Japan*, 1934, **54**, 154.
[2] Takiura, *J. Pharm. Soc. Japan*, 1941, **61**, 475.
[3] Takiura, personal communication.
[4] (*a*) Takiura, *J. Pharm. Soc. Japan*, 1941, **61**, 482; 1943, **63**, 40; (*b*) Wessely and Wang, *Ber.*, 1940, **73**, 19; (*c*) Wessely and Bauer, *Ber.*, 1942, **75**, 617; (*d*) Wessely and Lauterbach, *Ber.*, 1942, **75**, 958.
[5] Thomson, " Naturally Occurring Quinones," Butterworths Sci. Publ. Ltd., London, 1957, p. 260.
[6] Todd, *Ann. Reports*, 1941, **38**, 209.

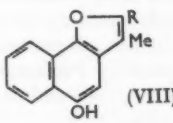
We were led by our interest in diterpene synthesis to attempt their synthesis and our initial aim was to prepare the fully aromatic tanshinone-I. In this we have been unsuccessful but we now record the synthesis of the isomer (IV).

A key intermediate in our proposed synthesis was the coumarin (V; R = OH, R′ = Cl or Br) which could be converted by standard methods into a hydroxyphenanthrofuran which should readily give the desired quinone by further oxidation. This key intermediate should be available from 1-hydroxy-8-methylphenanthrene (VI; R = H) by conversion into the coumarin (V; R = R′ = H) and subsequent Elbs persulphate oxidation and bromination. This route, though unambiguous, suffers from the disadvantage that the starting material is not readily available. Furthermore, a model experiment [7] with a simple analogue (VII; R = R′ = H) suggested that the Elbs oxidation of the pyrone (V; R = R′ = H) would be difficult. We accordingly attempted the synthesis of the intermediate pyrone (V; R = OH, R′ = Cl) directly from 1,4-dihydroxy-8-methylphenanthrene (VI; R = OH).

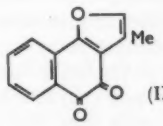
Model experiments with 1,4-dihydroxynaphthalene were encouraging. This compound was readily converted into the coumarin (VII; R = OH, R′ = Cl) by a Pechmann reaction with ethyl α-chloroacetoacetate, which in turn underwent ring contraction to the naphthofuran (VIII; R = $CO_2H$) with alkali. Oxidation with either selenium dioxide or, much better, potassium nitrosodisulphonate [8] then gave the *o*-quinone. Similar oxidation of the decarboxylated furan (VIII; R = H) was also satisfactory, and the product (IX) was reductively methylated to give an ether whose ultraviolet absorption closely resembled that of the leuco-dimethyl ether of tanshinone-II,[4d] confirming the supposition that they have a common chromophore.



(VII)



(VIII)



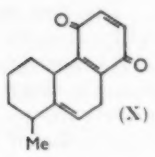
(IX)

The dihydroxymethylphenanthrene (VI; R = OH) needed for the synthesis has not been reported, but Robins and Walker [9] and Deno and Johnston [10] prepared the dione (X) by the Diels–Alder addition of benzoquinone to 3-methyl-2-vinylcyclohexene. We experienced some difficulty in repeating this preparation when using methanol as a solvent, as sometimes the only solid product was a high-melting non-ketonic material to which, on the basis of analysis and ultraviolet absorption, we assign the structure (XI). Robins [11] also had some failures with this reaction which he attributed to the presence of adventitious acid. When the addition was performed in benzene no difficulty was experienced. The diketone was rearranged to the quinol by short treatment with acid, and this was methylated, dehydrogenated, and demethylated to give the desired phenol. 1,4-Dihydroxyphenanthrene has been made by Grob *et al.*[12] in a similar way and we modified their method by carrying out the dehydrogenation with sulphur, which gives appreciably better yields than palladised charcoal.

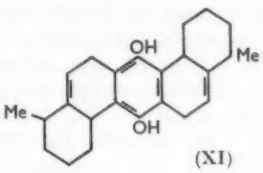
The Pechmann reaction with the diol (VI; R = OH) was expected to yield two products. Orientation effects might be expected to favour formation of the unwanted isomer (XII) but we hoped that they would not exclude the formation of appreciable amounts of the

[7] Bhevsar and R. D. Desai, *Indian J. Pharm.*, 1951, **13**, 200; cf. R. B. Desai and Sethna, *J. Indian Chem. Soc.*, 1951, **28**, 213.
[8] Teuber and Gotz, *Chem. Ber.*, 1954, **87**, 1236; 1956, **89**, 2654.
[9] Robins and Walker, *J.*, 1952, 642.
[10] Deno and Johnston, *J. Org. Chem.*, 1952, **17**, 1466.
[11] Robins, personal communication.
[12] Grob, Jundt, and Wicki, *Helv. Chim. Acta*, 1949, **32**, 2427.

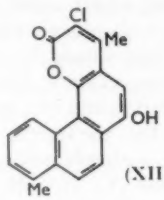
desired isomer (V; R = OH, R′ = Cl). We had expected to be able to separate the two possible products at this stage and to proceed with each separately. However, it appears that only one product is formed and this was shown to have the structure (XII).




(X)




(XI)




(XII)

Ring contraction of the pyrone took place easily and the product, characterised as the *O*-methyl ether methyl ester, was decarboxylated on good yield. The orientation of the product was determined at this stage by vigorous catalytic reduction, followed by dehydration and dehydrogenation with selenium. Depending on the position of attachment of the original pyrone ring to the phenanthrene skeleton the product should be retene or 6-isopropyl-1-methylphenanthrene. The product actually obtained was not isolated pure but its m. p. of 31—32°, undepressed by admixture with 6-isopropyl-1-methylphenanthrene, m. p. 45° (kindly supplied by Professor S. N. Slater), and its ultraviolet absorption which was identical over all peaks (eleven) with that of the authentic sample, left little doubt that it was substantially the 6-isopropyl isomer, and that therefore the parent furan had the opposite orientation to that suggested for the tanshinones.

As expected, oxidation of the furan with potassium nitrosodisulphonate took place smoothly to give the quinone (IV), which was very similar in appearance to tanshinone-I. The melting point was close to that of the natural pigment but was depressed on admixture with an authentic sample (kindly supplied by Professor K. Takiura). The new quinone, which was characterised as the quinoxaline, showed distinct differences in its ultraviolet absorption from that of the natural product.

## Experimental

Except where otherwise indicated, ultraviolet absorption refers to ethanolic solutions. Light petroleum had b. p. 60—80°.

*3-Chloro-6-hydroxy-4-methyl-2-naphtho*[1,2-b]*pyrone* (VII; R = OH, R′ = Cl).—84% Sulphuric acid (100 c.c.) was slowly added to a cold (10°) stirred paste of 1,4-dihydroxynaphthalene (10 g.) and ethyl α-chloroacetoacetate (15 c.c.). Stirring was continued for 18 hr. and the mixture was then poured into water (200 c.c.). The brown precipitate was extracted with boiling glacial acetic acid (200 c.c.) to remove impurities and the crude residual *pyrone* (12·6 g.) was collected. Extraction with ethyl acetate removed further coloured impurities to give a very sparingly soluble, pale brown product, m. p. 305—307°. It crystallised from acetic acid as yellow prisms, m. p. 310—311° (Found: C, 64·2; H, 3·5; Cl, 13·0. $C_{14}H_9ClO_3$ requires C, 64·5; H, 3·5; Cl, 13·6%), $\lambda_{max.}$ (in $CHCl_3$) 282 (ε 23,000), 291 (ε 27,000), 316 (ε 6500), and 383 mμ (ε 6500).

*5-Hydroxy-3-methylnaphtho*[1,2-b]*furan-2-carboxylic Acid* (VIII; R = $CO_2H$).—The above naphthopyrone (6 g.) was heated under reflux with 10% ethanolic potassium hydroxide (220 c.c.) under nitrogen for 6 hr. The solution was then diluted with water and acidified with hydrochloric acid. The product was collected in ether, and the acidic portion extracted with aqueous sodium hydrogen carbonate and crystallised from acetic acid (charcoal) as blades, m. p. 254—255° (decomp.), yield 69%. This and all other carboxyfurans made in this investigation gave low carbon values on analysis. The acid with diazomethane gave the O-*methyl ether methyl ester* which crystallised from acetic acid as prisms, m. p. 234—235° (Found: C, 71·1; H, 5·1. $C_{16}H_{14}O_4$ requires C, 71·1; H, 5·2%).

*4,5-Dihydro-3-methyl-4,5-dioxonaphtho*[1,2-b]*furan-2-carboxylic Acid.*—(*a*) A solution of

potassium nitrosodisulphonate (0·45 g.) in water (30 c.c.) containing 0·65M-potassium dihydrogen phosphate (7·5 c.c.) was added to a solution of the above hydroxyfurancarboxylic acid (0·15 g.) in acetone (13 c.c.). After 12 hr. at room temperature the acetone was evaporated under reduced pressure and the aqueous residue was acidified with concentrated hydrochloric acid (2 drops) and left in the refrigerator for 8 hr. The precipitated orange *quinone* was collected and crystallised from ethanol and finally ethyl acetate as prisms, m. p. 292—293° (decomp.) (Found: C, 65·1; H, 3·3. $C_{14}H_8O_5$ requires C, 65·6; H, 3·1%), $\lambda_{max.}$ 255 (ε 24,000), 277 (ε 26,000), and 431 mμ (ε 2000). It dissolved in concentrated sulphuric acid to give a purple solution which changed to blue-green. *o*-Phenylenediamine in glacial acetic acid gave the *quinoxaline* as yellow needles (from dioxan), m. p. 310—312° (Found: N, 8·4. $C_{20}H_{12}N_2O_3$ requires N, 8·5%).

(*b*) A solution of the naphthofuroic acid (0·2 g.) in dioxan (15 c.c.) containing water (1 drop) and selenium dioxide (0·15 g.) was boiled for 4 hr. When cold the solution was filtered and diluted with water (15 c.c.), and the precipitated impurity was removed. The residual solution was acidified and after two days deposited the above quinone (30 mg.), m. p. and mixed m. p. 291—292° (decomp.).

5-*Hydroxy*-3-*methylnaphtho*[1,2-b]*furan* (VIII; R = H).—The above furoic acid (1·7 g.) and copper bronze (1·5 g.) were heated to 250°/12 mm. The temperature was slowly raised to 265° and the volatile product was collected on a cold finger. The *naphthofuran* was purified by sublimation at 135°/0·05 mm. It formed colourless needles, m. p. 145—146° (53%) (Found: C, 79·2; H, 5·3. $C_{13}H_{10}O_2$ requires C, 78·8; H, 5·1%).

4,5-*Dihydro*-3-*methyl*-4,5-*dioxonaphtho*[1,2-b]*furan* (IX).—The above furan (1·05 g.) was oxidised with potassium nitrosodisulphonate (3·2 g.) as described for the related acid above. The *quinone* (0·95 g.) crystallised from aqueous acetone as red blades, m. p. 168° (Found: C, 73·6; H, 3·8. $C_{13}H_8O_3$ requires C, 73·6; H, 3·8%), $\lambda_{max.}$ 247 (ε 19,000), 265 (ε 26,000), 270 (ε 22,000), 455 mμ (ε 2000). The derived *quinoxaline*, prepared in acetic acid, crystallised as yellow needles, m. p. 175° (from ethanol) (Found: C, 80·6; H, 4·2; N, 9·6. $C_{19}H_{12}N_2O$ requires C, 80·3; H, 4·25; N, 9·8%). A solution of the quinone in concentrated sulphuric acid was green, becoming purple and finally brown.

4,5-*Dimethoxy*-3-*methylnaphtho*[1,2-b]*furan*.—The last-mentioned quinone (0·4 g.) in ethanol (20 c.c.) was hydrogenated at room temperature and pressure over palladium black. 1 Mol. of hydrogen was absorbed, and dimethyl sulphate (20 c.c.) and 20% aqueous sodium hydroxide (40 c.c.) were then added. After 2·5 hr. the solution was diluted and extracted with ether, and the extract washed (dilute hydrochloric acid and water), dried and distilled. The fraction with b. p. 110—120° (bath)/0·08 mm. was filtered in light petroleum through a short column of alumina and redistilled [b. p. 118—122° (bath)/0·1 mm.]. The *dimethyl ether* so obtained solidified (m. p. 51—52°) but could not be crystallised (Found: C, 74·6; H, 5·9. $C_{15}H_{14}O_3$ requires C, 74·4; H, 5·8%); it had $\lambda_{max.}$ 259 (ε 30,000), 323 (ε 9000), 340 mμ (ε 4000).

1,2,3,4,6,7b,8,9,10,11,13,14b-*Dodecahydro*-7,14-*dihydroxy*-4,11-*dimethyldibenz*[a,h]*anthracene* (XI).—On some occasions a solution of the methylvinylcyclohexene mixture from the dehydration of 2-methyl-1-vinylcyclohexanol and benzoquinone in methanol deposited, not the Diels–Alder adduct, but the *dibenzanthracene derivative* which separated from light petroleum as colourless needles, m. p. 197—198° (Found: C, 82·3; H, 8·5. $C_{24}H_{30}O_2$ requires C, 82·2; H, 8·6%), $\lambda_{max.}$ 249 (ε 6700) and 299 mμ (ε 1300). Acetic anhydride in pyridine gave the *diacetate*, prisms (from ethanol), m. p. 223—225° (Found: C, 77·1; H, 7·8. $C_{28}H_{34}O_4$ requires C, 77·4; H, 7·9%).

5,6,7,8,10,13-*Hexahydro*-1,4-*dimethoxy*-8-*methylphenanthrene*.—The corresponding diphenol [10] (28 g.) was methylated by dimethyl sulphate (45 g.) and potassium carbonate (90 g.) in boiling acetone (1 l.) for 30 hr. Most of the acetone was then evaporated, the residue was diluted with water, and the product was collected with ether. The extract was washed with aqueous sodium hydroxide and then dilute hydrochloric acid and water, dried, and distilled. The *dimethyl ether* (29 g., 92%) distilled as a colourless oil, b. p. 148—149°/4·5 mm., which separated from acetone as large prisms, m. p. 66—67° (Found: C, 79·2; H, 8·8; OMe, 20·2. $C_{17}H_{22}O_2$ requires C, 79·0; H, 8·6; 2OMe, 19·4%).

1,4-*Dimethoxy*-8-*methylphenanthrene*.—The above dimethyl ether (1·6 g.) was heated with sulphur (0·6 g.) at 200—220° for 3 hr. The mixture was triturated with ethanol, and the solid product was chromatographed on alumina from which light petroleum–benzene (95 : 1) eluted the *dimethoxyphenanthrene* (1·0 g.); this crystallised from ethanol as needles, m. p. 124° (Found:



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C, 80·7; H, 6·5; OMe, 24·5. $C_{17}H_{16}O_2$ requires C, 80·9; H, 6·4; 2OMe, 24·6%), $\lambda_{max.}$ 240 (ε 52,000), 286 (ε 22,000), 309 (ε 10,000), 351 (ε 4500), and 368 mμ (ε 5000). The *picrate* formed brown needles (from ethanol), m. p. 168—170° (Found: C, 56·9; H, 4·1. $C_{17}H_{16}O_2,C_6H_3N_3O_7$ requires C, 57·4; H, 4·0%).

3-*Chloro*-6-*hydroxy*-4,9-*dimethyl*-2-*phenanthro*[4,3-b]*pyrone* (XII).—The above methyl ether (1·0 g.) was heated with pyridine hydrochloride (3·4 g.) at 170—190° for 4 hr. The addition of water then precipitated the phenanthrenediol (0·84 g.), sufficiently pure for use in the next stage. A paste of the diol (1 g.) and ethyl α-chloroacetoacetate (3·5 c.c.) was treated at 0° with 88% sulphuric acid (20 c.c.), and after 24 hr. at room temperature was diluted with water, to give the solid *chloropyrone* (100%) which sublimed at 210°/5 × $10^{-5}$ mm. as yellow needles, m. p. 280—300° (charring) (Found: C, 70·2; H, 4·2; Cl, 11·3. $C_{19}H_{13}ClO_3$ requires C, 70·3; H, 4·0; Cl, 10·9%), $\lambda_{max.}$ 257 (ε 35,000), 283 (ε 26,000), 340 (ε 9000), 353 (ε 10,000), 396 (ε 9000), and 413 mμ (9300).

5-*Hydroxy*-3,8-*dimethylphenanthro*[4,3-b]*furan*-2-*carboxylic Acid*.—The above chloropyrone (1·5 g.) was heated at the b. p. under nitrogen with alcoholic 10% potassium hydroxide (75 c.c.) for 5 hr. The solution was then diluted, acidified, and extracted with ether. The acidic part of the product was extracted from the ether with aqueous sodium hydrogen carbonate, and acid then liberated the furan-carboxylic acid as a flocculent precipitate (1·05 g.). Diazomethane gave the O-*methyl ether methyl ester* which separated from acetic acid as pale yellow prisms, m. p. 306—307° (decomp.) (Found: C, 75·1; H, 5·3. $C_{21}H_{18}O_4$ requires C, 75·4; H, 5·4%).

5-*Hydroxy*-3,8-*dimethylphenanthro*[4,3-b]*furan*.—The above acid (1·0 g.) and copper bronze (3 g.) were heated to 220°/14 mm. The temperature was raised during 30 min. to 280° and the crude *furan* was collected on a cold finger. Resublimation at 170°/0·1 mm. gave the product (0·49 g.) as needles, m. p. 223° (Found: C, 82·2; H, 5·5. $C_{18}H_{14}O_2$ requires C, 82·4; H, 5·4%).

*Orientation of* 5-*Hydroxy*-3,8-*dimethylphenanthro*[4,3-b]*furan*.—The above furan (0·25 g.) was hydrogenated in methylcyclohexane over Raney nickel at 200°/200 atm. for 3 hr. Removal of catalyst and solvent then left a clear oil transparent to ultraviolet light. This oil was dehydrated with potassium hydrogen sulphate at 180° for 30 min. and finally heated with selenium at 340—350° for 12 hr. Distillation then gave a product which crystallised from methanol and then aqueous ethanol as plates, m. p. 31—32°, raised to 32—34° on admixture with 6-isopropyl-1-methylphenanthrene (m. p. 45—46°). The ultraviolet spectrum of both hydrocarbons showed eleven peaks at the same wavelengths, the intensities of each peak also being nearly identical.

4,5-*Dihydro*-3,8-*dimethyl*-4,5-*dioxophenanthro*[4,3-b]*furan* (IV).—The above phenanthrofuran (100 mg.) was oxidised with potassium nitrosodisulphonate (0·38 g.) as previously described. The *quinone* crystallised from acetic acid as dark red prisms (98 mg.), m. p. 230—232°, raised to 233—234° by crystallisation from toluene (Found: C, 77·9; H, 4·7. $C_{18}H_{12}O_3$ requires C, 78·2; H, 4·4%). The m. p. was depressed to 194—202° on admixture with tanshinone-I (m. p. 230—231°). The derived *quinoxaline* was formed in acetic acid and crystallised from ether as yellow needles, m. p. 252—253° (Found: C, 82·3; H, 4·5; N, 8·15. $C_{24}H_{16}N_2O$ requires C, 82·7; H, 4·6; N, 8·05%); tanshinone-I quinoxaline has m. p. 231°. The ultraviolet spectrum of the quinone (in $CH_2Cl_2$) had $\lambda_{max.}$ 230 (ε 28,000), 295 (ε 30,000), 305 (ε 29,000), 364 (ε 4000), and 540 mμ (ε 3000); under the same conditions tanshinone-I had peaks at 245 (ε 39,000), 280 (ε 20,000) and 418 mμ (ε 6000).

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## 1009. *Reaction of* L-*Threitol with Acetone.*

By A. B. Foster, A. H. Olavesen, and J. M. Webber.

On acid-catalysed reaction with acetone, L-threitol affords mainly the 1,2:3,4-di-*O*-isopropylidene derivative, together with a small amount of the 1,2-*O*-isopropylidene compound (isolated as the di-*O*-*p*-phenylazobenzoate).

In the acid-catalysed reaction of acetone with acyclic polyhydric alcohols, condensation usually involves terminal vicinal (α in Barker and Bourne's terminology [1]) and *threo*-diol groups (αT). Apparently no example has been recorded where *erythro*-diol groups (αC) are involved although simpler compounds such as *erythro*-1,2-diphenylethane-1,2-diol are known to condense with acetone.[2] Further, it is known [3] that α-rings may be formed more readily than αT-rings and that in compounds containing both types of ring the latter are more stable towards acid. It was therefore of interest to examine the acetone threitol reaction since, if formation of 1,3-dioxolan derivatives is assumed,[3,4] a competitive reaction is theoretically possible involving the formation of a di-*O*-isopropylidene derivative (two α-rings) and/or two mono-*O*-isopropylidene derivatives (α- and αT-ring).

When L-threitol, obtained by acidic hydrolysis of 1,3-*O*-benzylidene-L-threitol,[5] was treated with acetone and sulphuric acid under conditions where erythritol gave *ca.* 95% of the di-*O*-isopropylidene compound, the main product (*ca.* 80%) was also a di-*O*-isopropylidene derivative. The small amount of mono-*O*-isopropylidene derivative formed was isolated as the di-*O*-*p*-phenylazobenzoate, m. p. 198—199°, $[M]_{5461}$ −216° (in $CHCl_3$) which was clearly not enantiomorphous with 2,3-*O*-isopropylidene-1,4-di-*O*-*p*-phenylazobenzoyl-D-threitol {m. p. 192—194°, $[M]_{5461}$ +116° (in $CHCl_3$)}, obtained by sequential application of periodate oxidation, borohydride reduction, and *p*-phenylazobenzoylation to 3,4-*O*-isopropylidene-D-mannitol. The mono-*O*-isopropylidene derivative was identified as 1,2-isopropylidene-3,4-di-*O*-*p*-phenylazobenzoyl-L-threitol since its saponification gave a product which consumed 0·92 mol. of periodate and released 0·9 mol. of formaldehyde. Similar saponification of 2,3-*O*-isopropylidene-1,4-di-*O*-*p*-phenylazobenzoyl-D-threitol gave a product resistant to periodate oxidation.

Treatment of the di-*O*-isopropylidene-L-threitol with 70% acetic acid at 50° for 45 min. caused almost complete hydrolysis. However, the small amount of mono-*O*-isopropylidene derivative which survived was identified by conversion into 1,2-*O*-isopropylidene-3,4-di-*O*-*p*-phenylazobenzoyl-L-threitol, thereby indicating a 1,2:3,4-distribution of the cyclic ketal groups in the di-*O*-isopropylidene derivative. Thus, further support is provided for Barker and Bourne's contention [3] that α-ketal rings are formed in preference to αT-rings. Additionally, it seems likely that the products obtained [6] from erythritol are, respectively, 1,2:3,4-di-*O*-isopropylidene-erythritol and 1,2-*O*-isopropylidene-DL-erythritol.

Both L-threitol and erythritol gave crystalline tetra-*O*-*p*-phenylazobenzoates, further exemplifying [7] the value of this derivative for characterization.

### Experimental

Infrared spectra for comparative purposes were obtained by using a Perkin–Elmer 21 spectrometer. Optical rotations of *p*-phenylazobenzoates were determined at 5461 Å on a type 143A Ericsson automatic polarimeter with a path length of 1 cm. Periodate oxidations

[1] Barker and Bourne, *J.*, 1952, 905.
[2] Hermans, *Z. phys. Chem.*, 1924, **113**, 337.
[3] Barker and Bourne, *Adv. Carbohydrate Chem.*, 1952, **7**, 137.
[4] Mills, *Adv. Carbohydrate Chem.*, 1955, **10**, 1.
[5] Foster, Haines, Homer, Lehmann, and Thomas, *J.*, 1961, 5005.
[6] Speier, *Ber.*, 1895, **28**, 2531; Fischer and Rund, *Ber.*, 1916, **49**, 88.
[7] Baggett, Foster, Haines, and Stacey, *J.*, 1960, 3528.

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were performed essentially by Jackson's method,[8] and formaldehyde was determined by the chromotropic acid method.[9]

*Hydrolysis of* 1,3-O-*Benzylidene*-L-*threitol*.—A solution of 1,3-*O*-benzylidene-L-threitol (1·18 g.; m. p. 134—135°, obtained from 1,3-*O*-benzylidene-L-arabinitol [5]) in 0·5N-sulphuric acid was kept at 95—100° for 1 hr. The cooled solution was extracted with benzene to remove benzaldehyde, then neutralised with methyl di-n-octylamine [10] and concentrated. Recrystallization of the residue (0·595 g.) from ethanol gave L-threitol (0·188 g., 26%), m. p. 88—89°, $[M]_{5461}$ −7° (*c* 0·4 in $H_2O$). In a subsequent experiment the yield of purified L-threitol was 75%.

*Isopropylidene Derivatives of* L-*Threitol*.—A mixture of acetone (100 ml.), concentrated sulphuric acid (0·4 ml.), and L-threitol (0·99 g.) was shaken overnight at room temperature. The mixture was then poured with vigorous stirring into 2% aqueous potassium carbonate (100 ml.) at such a rate that an acid pH did not develop. The acetone was removed by concentration under diminished pressure and the remaining aqueous solution was extracted with chloroform (40 ml.). Concentration of the dried ($MgSO_4$) extract gave a residue (1·35 g.), the infrared spectrum (liquid film) of which showed only weak absorption for hydroxyl at 3400 $cm.^{-1}$. Recrystallization of the residue from light petroleum (b. p. 60—80°) gave *di*-O-*isopropylidene*-L-*threitol*, m. p. 34—35°, b. p. 80°/0·2 mm., $[\alpha]_{5461}$ +3° (*c* 0·7 in $CHCl_3$), $[M]_{5461}$ +6° (Found: C, 59·4; H, 8·9. $C_{10}H_{18}O_4$ requires C, 59·4; H, 8·9%).

Subsequent continuous extraction of the aqueous solution with chloroform for 20 hr. followed by concentration of the dried ($MgSO_4$) extract gave a residue (0·266 g.) which was clearly a mixture of mono- and di-*O*-isopropylidene derivatives since it had $\nu_{max.}$ for hydroxyl at 3350 $cm.^{-1}$ but consumed only 0·6 mol. of periodate, releasing 0·6 mol. of formaldehyde. The latter value corresponds to an overall yield of *ca.* 11% of 1,2-*O*-isopropylidene-L-threitol. The mixture was *p*-phenylazobenzoylated in the usual way.[7] Recrystallization of the product from benzene–light petroleum (b. p. 60—80°) gave 1,2-O-*isopropylidene*-3,4-*di*-O-p-*phenylazobenzoyl*-L-*threitol*, m. p. 198—199°, $[\alpha]_{5461}$ −37° (*c* 0·4 in $CHCl_3$), $[M]_{5461}$ −216° (Found: C, 68·5; H, 5·3; N, 9·7. $C_{33}H_{30}N_4O_6$ requires C, 68·5; H, 5·2; N, 9·7%).

Under the same conditions erythritol (1·05 g.) gave crude crystalline di-*O*-isopropylidene derivative (1·6 g., 98%) which had m. p. 55—56° after recrystallization from ether–light petroleum (b. p. 60—80°).

*Saponification and Periodate Oxidation of* 1,2-O-*Isopropylidene*-3,4-O-p-*phenylazobenzoyl*-L-*threitol*.—A mixture of the di-*O*-*p*-phenylazobenzoate (35 mg.), ethanol (5 ml.), and potassium hydroxide (0·125 g.) was boiled for 5 hr. The solution was stored at 0° overnight, the potassium *p*-phenylazobenzoate was removed, and the filtrate was evaporated to dryness at *ca.* 50°/~12 mm. A solution of the residue in water (20 ml.) was extracted continuously with chloroform for 12 hr. and the dried ($MgSO_4$) extract was evaporated, yielding crude 1,2-*O*-isopropylidene-L-threitol (10 mg.). This compound consumed 0·92 mol. of periodate in <30 min. and none subsequently, and 0·9 mol. of formaldehyde was released.

After hydrolysis of the 1,2-*O*-isopropylidene-L-threitol with N-hydrochloric acid at 95—100° for 1 hr., the neutralized hydrolysate consumed 2·2 mol. of periodate, releasing 1·36 mol. of formaldehyde, corresponding to a ratio of oxidant consumed : formaldehyde released of 3 : 1·9. The expected ratio was 3 : 2.

Saponification of 2,3-*O*-isopropylidene-1,4-di-*O*-*p*-phenylazobenzoyl-D-threitol by the same procedure gave a product resistant to periodate oxidation. Further acidic hydrolysis gave a product for which the ratio oxidant consumed : formaldehyde released was 3 : 1·6.

*Graded Acidic Hydrolysis of Di*-O-*isopropylidene*-L-*threitol*.—A solution of the di-*O*-isopropylidene derivative (0·6 g.) in water (6 ml.) and acetic acid (14 ml.) was kept at 50° for 45 min. and then rapidly neutralized with 2N-sodium hydroxide. Extraction of the cooled solution with chloroform gave a small amount (18 mg.) of (presumably) starting material. Subsequent continuous extraction with chloroform for 40 hr. gave a product (26 mg.) which was esterified with *p*-phenylazobenzoyl chloride (0·2 g.) and pyridine (10 ml.) at 95—100° for 3 hr. The mixture was worked up in the standard manner [7] and afforded a product (0·1 g.) which on recrystallization from benzene–light petroleum (b. p. 60—80°) gave 1,2-*O*-isopropylidene-3,4-di-*O*-*p*-phenylazobenzoyl-L-threitol (60 mg.), m. p. 192—194°, $[\alpha]_{5461}$ −39°

[8] Jackson, *Org. Reactions*, 1944, **2**, 341.
[9] O'Dea and Gibbons, *Biochem. J.*, 1953, **55**, 580.
[10] Lester-Smith and Page, *J. Soc. Chem. Ind.*, 1948, **67**, 48.

(*c* 0·3 in $CHCl_3$), $[M]_{5461}$ −225°. The m. p. was undepressed on admixture with the authentic compound described above and the infrared spectra (KBr discs) of these compounds were indistinguishable.

*Periodate Oxidation of* 3,4-O-*Isopropylidene*-D-*mannitol*.—(*a*) A solution (50 ml.) of the isopropylidene compound (50 mg.) and sodium metaperiodate (0·27 g.) in water at room temperature consumed 1·95 mol. of oxidant after 4 min. and 2·03 mol. after 29 min. No further uptake was observed.

(*b*) A solution of the monoisopropylidene compound (1 g.) and sodium metaperiodate (5 g.) in water (*ca.* 150 ml.) was shaken for 1 hr. and then neutralised with barium hydroxide. Insoluble material was removed and sodium borohydride (2 g.) was added to the aqueous solution. After 12 hr. at room temperature, the pH of the solution was adjusted to 7·5 with acetic acid. The solution was concentrated and then continuously extracted with chloroform for 2 days. Concentration of the dried ($MgSO_4$) extract gave crude 2,3-*O*-isopropylidene-L-threitol (0·19 g.). The aqueous solution was freeze-dried and the residue was extracted with hot ethyl acetate. Concentration of the extract gave a further amount (0·38 g., total yield 79%) of the product which proved difficult to recrystallize. It was resistant to periodate oxidation. A portion was therefore *p*-phenylazobenzoylated yielding 2,3-O-*isopropylidene*-1,4-di-O-p-*phenylazobenzoyl*-D-*threitol*, m. p. 192—194° (from benzene–light petroleum), $[\alpha]_{5461}$ +20° (*c* 0·3 in $CHCl_3$), $[M]_{5461}$ +116° (Found: C, 68·3; H, 5·3; N, 9·6. $C_{33}H_{30}N_4O_6$ requires C, 68·5; H, 5·2; N, 9·7%).

p-*Phenylazobenzoylation of the Tetritols*.—A mixture of L-threitol (50 mg.), *p*-phenylazobenzoyl chloride (0·48 g.), and dry pyridine (20 ml.) was kept at 95—100° for 3 hr. and then worked up in the usual way,[7] to yield the *tetra*-O-p-*phenylazobenzoate* (0·32 g., 82%), m. p. 207—208° (from benzene–light petroleum), $[\alpha]_{5461}$ −36° (*c* 0·3 in $CHCl_3$), $[M]_{5461}$ −340° (Found: C, 70·3; H, 4·6; N, 11·5. $C_{56}H_{42}N_8O_8$ requires C, 70·5; H, 4·4; N, 11·7%). Likewise, erythritol gave a *tetra*-O-p-*phenylazobenzoate*, m. p. 186—187° (Found: C, 70·4; H, 4·9%).

The authors thank Professor M. Stacey, F.R.S., for his interest and the D.S.I.R. for a grant for the purchase of the automatic polarimeter.

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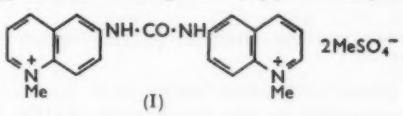
## 1010. *The Search for Chemotherapeutic Amidines. Part XIX.* 3,3′-Diamidinocarbanilide and its Congeners.*

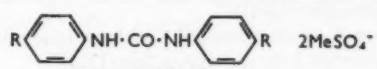
By S. S. BERG.

The preparation of 3,3′-diamidinocarbanilide di-isethionate, a new babesicidal drug, is described. Modifications to its structure have produced compounds of lower activity.

THE activity of ureas against babesial infections in cattle, sheep, horses, and goats has been reported by Schönhofer and Henecka [1] and by Mack.[2] The bisquinolinium urea ("Quinuronium sulphate") (I) is widely used in the treatment of natural infections of




(I)




(II) R = $NMe_3^+$
(III) R = $NMePr_2^+$

bovine redwater, and the carbanilides (II) and (III) have recently been developed in the U.S.S.R.

* Part XVII, Berg. *J.*, 1960, 5172; Part XVIII, Easson, *J.*, 1961, 1029.

[1] Schönhöfer and Henecka, Fiat Review of German Science, "Chemotherapy," 1939—1946, Vol. XLIII, p. 57.

[2] Mack, *Vet. Rev. Annot.*, **3**, 57.

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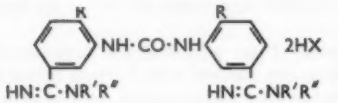
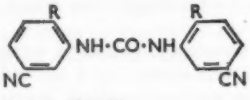
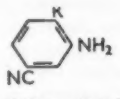
In view of the antiprotozoal activity of many aromatic diamidines, and the use of 4,4′-diamidinodiphenyl ether (phenamidine) in the treatment of canine babesiasis, it seemed desirable to examine a series of diamidinocarbanilides for babesicidal activity. 4,4′-Diamidinocarbanilide diacetate was shown to be inactive against *Babesia rodhaini* in



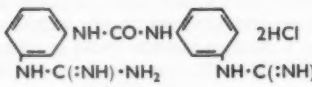

(IV)



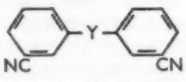

(V) a: R = H
b: R = Cl
c: R = OMe



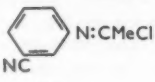

(VI) a: R = H
b: R = Cl
c: R = OMe



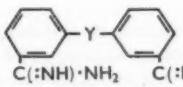

(VII)




(VIII) a: Y = NH·C(:NH)·NH
b: Y = N:CMe·NH
c: Y = NH·CS·NH




(X)




(IX) a: Y = NH·C(:NH)·NH
b: Y = N:CMe·NH
c: Y = NH·CS·NH

mice at half the lethal dose. The *meta*-isomer (IV; R = R′ = R″ = H, X = Cl), however, showed considerable activity in the screening test, and subsequent investigations were therefore confined to *meta*-amidines.

The dicyano-compounds (Va–c) were prepared by condensating the appropriate aminobenzonitrile (VIa–c) with carbonyl chloride in pyridine. They were converted into the di-imidates and thence into the diamidines. The latter were tested biologically as their water-soluble dihydrochlorides, dihydrobromides, or di-isethionates.

An alternative preparation by the reaction of *m*-aminobenzamidine monohydrochloride with carbonyl chloride or 3,5-dimethylpyrazole-1-carboxyamide gave a poor yield only of the diamidine (IV; R = R′ = R″ = H, X = Cl), and none was obtained by fusion of this amine with urea.

In an attempt to improve the chemotherapeutic properties of the compound (IV; R = R′ = R″ = H, X = Cl or $HO{\cdot}CH_2{\cdot}CH_2{\cdot}SO_3$) the following modifications were made to the structure of the diamidine: (1) The amidino-groups were replaced by other basic groups, (2) the urea linkage was replaced by related groups, and (3) substituents were introduced into the benzene rings. All of these modifications gave compounds of lower babesicidal activity.

Fusion of *m*-aminodimethylaniline with urea gave 3,3′-bisdimethylaminocarbanilide which gave a diquaternary salt with methyl sulphate.

3,3′-Diaminocarbanilide dihydrochloride was condensed with cyanamide to give the diguanidine (VII).

*m*-Aminobenzonitrile with cyanogenbromide gave the dinitrile (VIIIa) which was converted into the diamidine (IXa).

Reaction of *m*-acetamidobenzonitrile with phosphorus pentachloride gave the imidoyl chloride (X) which condensed with *m*-aminobenzonitrile to give the dinitrile (VIIIb) and thence the diamidine (IXb). The thiocarbanilide (VIIIc) was similarly prepared from *m*-aminobenzonitrile and thiocarbonyl chloride. Attempts to convert it into the diamidine (IXc) by the Pinner method,[3] or by direct fusion with ammonium benzenesulphonate, caused profound decomposition. No reaction occurred between *m*-aminobenzamidine monohydrochloride and 3,5-dimethylpyrazole-1-thiocarboxyamide.

[3] Ashley, Barber, Ewins, Newbery, and Self, *J.*, 1942, 103.

3,3′-Diamidino- and 3,3′-di-(*N*-methylamidino)-carbanilide dihydrochlorides were the most active compounds in mice in the screening test. As the former compound was the least toxic to calves, it was chosen for field trial. The activity of its di-isethionate against *Babesia divergens* in calves has been reported by Ashley *et al.*[4] and its efficacy in the field treatment of cattle in veterinary practice by Beveridge *et al.*[5]

TABLE 1.

Activity of some *mm′*-diamidines (2-R,5-R′-$C_6H_3$·NH)$_2$CO against *Babesia rodhaini* in mice.

| 2-Subst. | 5-Subst. | $LD_{50}$ (mg./g.) subcutaneous | $ED_{50}$ (mg./g.) subcutaneous |
|---|---|---|---|
| H | ·C(:NH)·$NH_2$ | 0·08 | 0·0038 |
| H | ·C(:NH)·NHMe | 0·1 | 0·0011 |
| OMe | ·C(:NH)·$NH_2$ | 0·3 | 0·082 |
| H | ·NH·C(:NH)·$NH_2$ | 0·1 | 0·046 |

The activity of the more active compounds against *Babesia rodhaini* in mice is summarised in Table 1; the biological data were kindly supplied by Mr. J. M. S. Lucas of the Veterinary Research Division.

## EXPERIMENTAL

*3,3′-Dicyanocarbanilides* (V).—Carbonyl chloride (1 mole) in anhydrous toluene (450 ml.) was added during 0·5 hr. to a stirred solution of the appropriate aminobenzonitrile (1·9 moles) in anhydrous pyridine (925 ml.). The exothermic reaction was controlled and the temperature kept below 30° by cooling in ice. Then the mixture was stirred for 0·5 hr. at 95—100°. After being cooled to 40°, it was added to ice-water (5·3 l.), and the precipitate was filtered off, washed with water, and crystallised. The results are recorded in Table 2.

*3,3′-Dicyanothiocarbanilide.*—This was prepared similarly from *m*-aminobenzonitrile (3·5 g.) and thiocarbonyl chloride (0·95 ml.) as pink prisms (1·8 g., 41%), m. p. 163° (from ethanol or ethyl acetate). It contained traces of solvent which could not be removed below the decomposition point (Found: C, 63·9; H, 4·0; N, 18·6; S, 10·9; Ac, 3·4. $C_{15}H_{10}N_4S$,0·25$C_4H_8O_2$ requires C, 64·0; H, 4·0; N, 18·7; S, 10·7; Ac, 3·6%).

NN′-*Di*-m-*cyanophenylguanidine.*—*m*-Aminobenzonitrile (23·6 g.) and cyanogen bromide (10·6 g.) in anhydrous ethanol (100 ml.) were refluxed overnight. Ether (4 vol.) was added to the cold reaction mixture, and the solid was filtered off and ground with 2N-sodium hydroxide. The *dinitrile* crystallised from aqueous ethanol as cream needles (15·2 g., 58%), m. p. 162—163° (Found: C, 69·1; H, 4·25; N, 26·8. $C_{15}H_{11}N_5$ requires C, 68·95; H, 4·25; N, 26·8%).

NN′-*Di*-m-*cyanophenylacetamidine.*—*m*-Acetamidobenzonitrile (23 g.) (Bogert and Kohnstamm [6]) was added to a solution of phosphorus pentachloride (30·1 g.) in anhydrous benzene (288 ml.) which was cooled with water. The mixture was refluxed for 0·25 hr., a clear

TABLE 2.

Dicyano-compounds (V).

| R | Yield (%) | Cryst. from | Crystalline form | M. p. | Found (%) C | H | N | Formula | Required (%) C | H | N |
|---|---|---|---|---|---|---|---|---|---|---|---|
| H | 77 | EtOH | Pink prisms | 205—206° | 68·4 | 3·9 | 21·8 | $C_{15}H_{10}N_4O$ | 68·7 | 3·8 | 21·4 |
| Cl[a] | 43·5 | $NMe_2$·CHO | White needles | 330 (decomp.) | — | — | 16·9 | $C_{15}H_8Cl_2N_4O$[c] | — | — | 16·9 |
| OMe[b] | 84·8 | ,, | Yellow needles | 315—316 | 64·0 | 4·6 | 17·4 | $C_{17}H_{14}N_4O_2$ | 63·35 | 4·35 | 17·4 |

[a,b] Prepared by Blanksma and Petri's method (*Rec. Trav. chim.*, 1947, **66**, 365); (*a*) m. p. 93—94°; (*b*) m. p. 84°. [c] Found: Cl, 21·4. Reqd.: Cl, 21·45%.

solution being obtained. The solvent was distilled off under reduced pressure from a bath at 50°, and anhydrous benzene (432 ml.) was added. *m*-Aminobenzonitrile (17·3 g.) in anhydrous

[4] Ashley, Berg, and Lucas, *Nature*, 1960, **185**, 461.
[5] Beveridge, Thwaite, and Shepherd, *Vet. Rec.*, 1960, **72**, 383.
[6] Bogert and Kohnstamm, *J. Amer. Chem. Soc.*, 1903, **25**, 482.

XUM

TABLE 3.

Diamidines, {5-[NR′R″·C(:NH)],2-R-$C_6H_3$}$_2$Y,2HX,$x$$H_2O$.

| No. | Y | R | R′ | R″ | X | $x$ | Alcohol and solvent for imidate prep. | Cryst. solvent | Form | Decomp. pt. | Yield (%) |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | NH·CO·NH | H | H | H | Cl | 1 | EtOH–$CHCl_3$ | MeOH–$COMe_2$ | Needles | 286° | 79 |
| 2 | NH·CO·NH | H | H | H | $C_2H_5O_4S$ [a] | 0 | EtOH–$CHCl_3$ | MeOH–$COMe_2$ | Needles | 256 (m. p. 209—210) | 78 |
| 3 | NH·CO·NH | H | Me | H | Cl | 1·5 | EtOH–$CHCl_3$ | 3N-HCl | Needles | 273—274 (soften 210) | 62 |
| 4 | NH·CO·NH | H | Et | H | Br | 1 | EtOH–$CHCl_3$ | MeOH–$COMe_2$ | Prisms | 302—305 | 32 |
| 5 | NH·CO·NH | H | Me | Me | Br | 1·75 | EtOH–$CHCl_3$ | Aq.NaBr | Needles | 300—302 | 48·6 |
| 6 | NH·CO·NH | Cl | H | H | Cl | 1 | HO·$[CH_2]_2$·OEt | 2N-HCl | Prisms | 280—282 | 21 |
| 7 | NH·CO·NH | OMe | H | H | Cl | 1 | HO·$[CH_2]_2$·OEt | N-HCl | Needles | 285—286 | 39·5 |
| 8 | NH·C(:NH)·NH | H | H | H | Cl [b] | 2 | HO·$[CH_2]_2$·OEt | MeOH–EtOAc | — | 254 | 55·6 |
| 9 | N:CMe·NH | H | H | H | Cl [b] | 0·5 | EtOH–$CHCl_3$ | MeOH–$COMe_2$ | — | 357 | 27·5 |

[a] Isethionate. [b] Contains 2·25HCl.

| No. | Found (%) C | H | Hal | N | $H_2O$ | Formula | Required (%) C | H | Hal | N | $H_2O$ |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 46·3 | 5·25 | 18·4 | 22·0 | 4·85 | $C_{15}H_{16}N_6O,2HCl,H_2O$ | 46·5 | 5·2 | 18·35 | 21·7 | 4·65 |
| 2 | — | — | — | 15·1 | — | $C_{15}H_{16}N_6O,2C_2H_6O_4S$ [c] | — | — | — | 15·3 | — |
| 3 | — | — | 16·6 | 20·1 | 6·0 | $C_{17}H_{20}N_6O,2HCl,1·5H_2O$ | — | — | 16·8 | 19·8 | 6·4 |
| 4 | — | — | 30·5 | 15·6 | 3·4 | $C_{19}H_{24}N_6O,2HBr,H_2O$ | — | — | 30·0 | 15·7 | 3·4 |
| 5 | — | — | 29·9 | 15·6 | 5·6 | $C_{19}H_{24}N_6O,2HBr,1·75H_2O$ | — | — | 29·2 | 15·4 | 5·8 |
| 6 | — | — | 31·2 | 18·9 | 3·85 | $C_{15}H_{14}Cl_2N_6O,2HCl,H_2O$ | — | — | 31·15 | 18·4 | 3·95 |
| 7 | — | — | 15·6 | 18·7 | 3·9 | $C_{17}H_{20}N_6O_3,2HCl,H_2O$ | — | — | 15·8 | 18·8 | 4·0 |
| 8 | 43·8 | 6·0 | 19·4 | 23·2 | 9·0 | $C_{15}H_{17}N_7,2·25HCl,2H_2O$ | 43·8 | 5·6 | 19·4 | 23·7 | 8·7 |
| 9 | 50·2 | 5·65 | 20·4 | 21·9 | 2·3 | $C_{16}H_{16}N_6,2·25HCl,0·5H_2O$ | 50·2 | 5·55 | 20·55 | 22·0 | 2·3 |

[c] Found: S, 11·6. Reqd.: S, 11·7%.

benzene (144 ml.) was slowly added to the stirred boiling solution of the imidoyl chloride, and a solid separated. After being refluxed for a further 3 hr., the mixture was cooled to 20°, and the solid was filtered off and dissolved in pyridine (575 ml.). Water (1725 ml.) was added to the filtered solution. The precipitate crystallised from ethanol as cream prisms (24·4 g., 65·3%), m. p. 186—188° (Found: C, 73·5; H, 4·8; N, 21·5. $C_{16}H_{12}N_4$ requires C, 73·85; H, 4·6; N, 21·55%).

The *diamidines* in Table 3 were prepared from the respective dicyano-compounds by the Pinner method (cf. Ashley *et al.*[3]).

*Reaction of* m-*Aminobenzamidine Monohydrochloride with Carbonyl Chloride.*—A suspension of finely powdered *m*-aminobenzamidine monohydrochloride (3·65 g.) (Easson and Pyman [7]) in anhydrous pyridine (15 ml.) was treated at 5—10° with a solution of carbonyl chloride (0·75 ml.) in anhydrous toluene. There was mildly exothermic reaction and a brown gum separated. After being heated for 0·5 hr. on a steam bath, the mixture was cooled to 25°, and the liquor was decanted from the gum. Addition of ether to an ethanolic solution of the gum gave a sticky solid, which was crystallised twice from 2N-hydrochloric acid to give 3,3′-diamidinocarbanilide dihydrochloride hydrate (0·24 g., 7%), white needles, decomp. 286°.

*Reaction of* m-*Aminobenzamidine Monohydrochloride with* 3,5-*Dimethylpyrazole*-1-*carboxyamide.*—*m*-Aminobenzamidine monohydrochloride (3·45 g.) and 3,5-dimethylpyrazole-1-carboxyamide (1·4 g.) (Scott *et al.*[8,9]) were refluxed in 2-ethoxyethanol (7 ml.) for 5 hr. After being cooled, the precipitate was filtered off; it crystallised from 2N-hydrochloric acid to give 3,3′-diamidinocarbanilide dihydrochloride hydrate (0·35 g., 8·75%) as white needles, decomp. 286°.

[7] Easson and Pyman, *J.*, 1931, 2991.
[8] Scott, *J. Amer. Chem. Soc.*, 1953, **75**, 1294, 4053.
[9] Scott, O'Donovan, Kennedy, and Reilly, *J. Org. Chem.*, 1957, **22**, 820.

XUM

*Attempted Preparation of 3,3′-Diamidinothiocarbanilide.*—(*a*) A suspension of 3,3′-dicyanothiocarbanilide (1·3 g.) in anhydrous chloroform (13 ml.) containing anhydrous ethanol (2 ml.) was saturated at 0° with anhydrous hydrogen chloride, a clear solution being obtained. After 7 days, a trace of insoluble material was filtered off, and the filtrate was diluted with anhydrous ether; this gave a foul-smelling gum. Attempts to isolate a pure imidate from the gum were unsuccessful. (*b*) A mixture of the dicyano-compound (1·5 g.) and ammonium benzenesulphonate (1·8 g.) was heated at 150°; profound decomposition occurred. At lower temperatures no reaction occurred. (*c*) *m*-Aminobenzamidine monohydrochloride (2·2 g.) and 3,5-dimethylpyrazole-1-thiocarboxyamide (1·0 g.) (Scott *et al.*[9]) in 2-ethoxyethanol (10 ml.) were refluxed for 5 hr. The solution was concentrated under reduced pressure, and the residual gum was dissolved in water. Addition of sodium bromide to the filtered solution precipitated *m*-aminobenzamidine monohydrobromide (2·0 g.), m. p. 72°.

*3,3′-Diguanidinocarbanilide Dihydrochloride Hemihydrate.*—3,3′-Diaminocarbanilide dihydrochloride (20 g.) (Brunner [10]), cyanamide (7 g.), and ethanol (53 ml.) were refluxed together overnight, a solution being obtained after 4 hr. The solid, which separated from the cold solution was filtered off and recrystallised from methanol–acetone. The *product* (12·8 g., 31·6%) separated as grey prisms, decomp. 270—272° (Found: Cl, 17·0; N, 27·2; $H_2O$, 2·4. $C_{15}H_{18}N_8O,2HCl,0{\cdot}5H_2O$ requires Cl, 17·4; N, 27·45; $H_2O$, 2·25%).

*3,3′-Bisdimethylaminocarbanilide.*—*m*-Aminodimethylaniline (31·3 g.) (Jaubert [11]) and urea (7 g.) were fused together at 148—152° for 2 hr. The solid was cooled and ground with ethanol. Crystallisation of this solid from 2-ethoxyethanol gave the *product* (14·8 g., 43·3%) as needles, m. p. 260—262° (Found: C, 67·65; H, 7·7; N, 18·5. $C_{17}H_{22}N_4O$ requires C, 67·5; H, 7·3; N, 18·5%). This with methyl sulphate in nitrobenzene gave the *dimethosulphate dihydrate*, plates (from methanol), decomp. 214—216° (Found: N, 9·45; S, 11·1; $H_2O$, 6·1. $C_{19}H_{28}N_4O^{2+},2CH_3SO_4^-,2H_2O$ requires N, 9·55; S, 10·9; $H_2O$, 6·15%).

The author thanks Dr. H. J. Barber, F.R.I.C., and Dr. J. N. Ashley, F.R.I.C., for their interest, and Mr. S. Bance, B.Sc., F.R.I.C., for the semimicroanalyses.

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[*Received, July 7th*, 1961.]

[10] Brunner, U.S.P. 2,503,797/1950.
[11] Jaubert, *Bull. Soc. chim. France*, 1899, **21**, 20.

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## 1011. *Substituted Benzidines and Related Compounds as Reagents in Analytical Chemistry. Part XVII.* The NNN′N′-Tetracarboxymethyl Derivatives of Some 3,3′-Disubstituted Benzidines.*

By D. I. REES and W. I. STEPHEN.

*NNN′N′*-Tetracarboxymethyl derivatives of some 3,3′-disubstituted benzidines have been prepared and their properties as analytical reagents have been examined. The dimethoxy- and diethoxy-derivatives are particularly useful as metallofluorescent indicators in the titration of copper(II) and mercury(II) with ethylenediaminetetra-acetic acid (EDTA). A similar but less sensitive reaction is shown by 3,3′-dicarboxybenzidine-*NNN′N′*-tetra-acetic acid in the titration of calcium with EDTA.

MANY compounds possessing the characteristic group $-N(CH_2{\cdot}CO_2H)_2$ have found extensive application as analytical reagents because of their ability to form complex compounds with many cations. The introduction of this group into the molecule of an acid–base indicator can result in the formation of an indicator suitable for complexometric titrations with EDTA.[1] Its effect on redox indicators and, in particular, the 3,3′-disubstituted derivatives of benzidine, which have recently been shown to have interesting redox

* Part XVI, *J.*, 1960, 4225.

[1] Schwarzenbach, Kampitsch, and Steiner, *Helv. Chim. Acta*, 1945, **28**, 828; Körbl and Pribil, *Chem. and Ind.*, 1957, 233; Belcher, Leonard, and West, *J.*, 1958, 2390.

XUM

properties,[2] was thought to be of interest. Accordingly, the *NNN'N'*-tetracarboxymethyl derivatives of benzidine, *o*-dianisidine, *o*-diphenetidine, *o*-tolidine, and benzidine-3,3'-disulphonic, -3,3-dicarboxylic, and -3,3'-di(oxyacetic acid) have been prepared. The preparation of the tetracarboxymethyl derivatives of 3,3'-dichloro-, 3,3'-dihydroxy-, and 3,3'-diamino-benzidine by a similar procedure was not at all satisfactory and these substances have not been included in the present study.

Condensation of sodium chloroacetate with organic amines has been extensively used by Schwarzenbach and others for the preparation of many aminocarboxylic acids, although this reaction has not been used with diamines of the benzidine type. Benzidine-*NN*-diacetic acid and -*NNN'N'*-tetra-acetic acid had been prepared by Reissert [3] in 1914. When these two polyacids were prepared according to his directions, they were obtained in a very impure state and were easily oxidised by air. Similarly, when *o*-dianisidine-*NNN'N'*-tetra-acetic acid was prepared by the original method, considerable difficulty was experienced in isolating the free acid in pure form because of its hygroscopic nature and lack of crystallinity. The isolation of these polyacids as sodium salts proved more satisfactory and it was possible to obtain tetrasodium *o*-dianisidinetetra-acetate as a stable, water-soluble, white powder. A general procedure was developed for the preparation of the tetrasodium salts of the various complexans based on these observations. This involved very slow addition of a solution of sodium chloroacetate in slight excess to an aqueous suspension of the appropriate benzidine at 100°, whilst the reaction mixture was stirred and maintained at pH 8 by addition of a solution of sodium carbonate. The product is then isolated as barium salt; this is converted into the sodium salt which is precipitated from water by a large excess of ethanol. A disadvantage of this procedure is that the product contains a small amount of sodium carbonate which cannot successfully be removed without appreciable loss. This residual inorganic matter has no effect on the analytical uses of the material.

An alternative to repeated crystallisation was developed for purification of tetrasodium *o*-dianisidine-*NNN'N'*-tetra-acetate. A slow stream of hydrogen chloride was passed through a suspension of the slightly impure sodium salt in cold ethanol; sodium chloride was filtered off, the excess of hydrogen chloride removed by concentration *in vacuo*, a solution of sodium ethoxide was added, and the precipitate of tetrasodium salt collected. This procedure could doubtless be used for other complexans of this type.

3,3'-Disulpho-*o*-dianisidine-, *o*-diphenetidine-, and -benzidine-*NNN'N'*-tetra-acetic acid and 3,3'-di(carboxymethoxy)benzidine-*NNN'N'*-tetra-acetic acid show intense fluorescences at pH 4—10 when their aqueous solutions are exposed to ultraviolet light. Although benzidine- and *o*-tolidine-*NNN'N'*-tetra-acetic acid also fluoresce over a wide pH range, the fluorescence is much weaker than that given by the above-mentioned compounds. The fluorescence of 3,3'-dicarboxybenzidine-*NNN'N'*-tetra-acetic acid is also fairly weak and only occurs above pH 7.

*Indicator Properties.*—The new derivatives reacted in a similar manner to the parent benzidines when treated with strong oxidising agents. Similarly coloured oxidation products to those given by the parent materials were obtained. The end-points obtained when the complexans were used as redox indicators in conventional titrations were very sluggish and their use in this connection was not further studied. Preliminary experiments indicated that the addition of various cations, especially $Cu^{2+}$, to aqueous solutions of the complexans had a pronounced effect on the fluorescence; with the *o*-dianisidine, *o*-diphenetidine, 3,3'-di(carboxymethyl)- and 3,3'-dicarboxy-benzidine derivatives the fluorescence was quenched completely. The derivatives of benzidine and tolidine are too weakly fluorescent for objective observation, whilst the fluorescence of 3,3'-disulphobenzidine-*NNN'N'*-tetra-acetic acid was only partially quenched by the addition of

[2] (*a*) Belcher, Nutten, and Stephen, *J.*, 1958, 2336; Rees and Stephen, *Talanta*, 1959, **2**, 361; (*b*) Rees and Stephen, *J.*, 1960, 4225.
[3] Reissert, *Ber.*, 1914, **47**, 679, 680.

metallic ions. These observations indicated that certain of these complexans might be applied as metallofluorescent indicators.

The substances were used initially as aqueous solutions of their sodium salts. However, the sharpness of the end-points deteriorated when these solutions were kept and it was necessary to prepare fresh solutions at least once a week. The solutions were more stable in dark bottles but it was more convenient to use the indicators as 1% solid mixtures with an inert salt such as sodium chloride or potassium nitrate.

A distinct advantage of the metallofluorescent indicator system is that the detection of the end-point is not affected by the colour of the solution, as happens with most of the metallochromic indicators.

*Titration of Copper.*—Solutions of copper(II) were titrated satisfactorily with EDTA when *o*-dianisidine-, *o*-diphenetidine-, and 3,3′-di(carboxymethoxy)benzidine-*NNN′N′*-tetra-acetic acid were used as indicators; the very sharp end-point was denoted by the appearance of fluorescence in solutions buffered over the pH range of 4—10. Slight overtitration occurred in the presence of the dioxyacetic acid derivative. 3,3′-Dicarboxybenzidine-*NNN′N′*-tetra-acetic acid gave an end-point only in solutions buffered to pH 10. An equally sharp end-point denoted by the disappearance of fluorescence was also obtained in the reverse titration. $Bi^{3+}$, $Cd^{2+}$, $Ce^{3+}$, $Ca^{2+}$, $Fe^{2+}$, $Fe^{3+}$, $Hg^{2+}$, $In^{3+}$, $La^{3+}$, $Ni^{2+}$, $Pb^{2+}$, $Th^{4+}$, $Tl^{3+}$, $Sn^{2+}$, and $Zr^{4+}$ interfere with the titration because they consume titrant. However, they do not affect the nature of the end-point, and so these ions can be titrated with an excess of EDTA, the excess being determined by titration with copper(II) in the presence of the metallofluorescent indicator. Since the indicators are themselves capable of binding metal ions, the indicator blank could be appreciable if the amount of indicator used were excessive; however, the fluorescence of these compounds is sufficiently intense to enable an amount of indicator equivalent only to a fraction of a drop of titrant to be used and this does not impair the quality of the end-point.

*Titration of Mercury.*—Stoicheiometric results were obtained in the titration of mercury(II) with EDTA at pH 4 when *o*-dianisidine-, and *o*-diphenetidine-*NNN′N′*-tetra-acetic acid were used as indicators. Although the end-points were not quite so sharp as those obtained in the titration of copper they were, nevertheless, quite distinct. The reverse titration was not so satisfactory because of the slight fluorescence that remained when a slight excess of mercury was present in the solution.

*Titration of Calcium.*—The fluorescence of 3,3′-dicarboxybenzidine-*NNN′N′*-tetra-acetic acid in alkaline solution was quenched by $Ca^{2+}$. Variable results were obtained initially in the titration of calcium with EDTA over the range pH 10—13 when an aqueous solution of the compound was used as indicator. Although the fluorescence of this solution was still intense a few days after its preparation, its indicator properties had disappeared, probably because of decarboxylation to the fluorescent *NNN′N′*-tetramethylbenzidine-3,3′-dicarboxylic acid. When the compound was used as a 1% solid mixture with sodium chloride this difficulty was overcome. However, there was still slight residual fluorescence in the presence of a small excess of calcium which is thought to be due to the presence of unchanged benzidine-3,3′-dicarboxylic acid. In spite of this, quite a sharp end-point was obtained with this indicator in the direct titration of calcium with EDTA in alkaline solution. Barium and strontium interfered, but one part of magnesium in ten parts of calcium could be tolerated.

*Electrophoretic Studies.*—With the exception of benzidine-*NNN′N′*-tetra-acetic acid and its 3,3′-dicarboxy-derivative the compounds gave a single intense blue fluorescent spot on paper electrophoresis at pH 10 (borate buffer). Benzidine-*NNN′N′*-tetra-acetic acid gave six fluorescent spots, the leading one being the most intense. Likewise, a complex pattern was obtained with 3,3′-dicarboxybenzidine-*NNN′N′*-tetra-acetic acid, but here no one spot was outstanding. The various blue-fluorescent bands which were obtained when a large amount of the latter material was subjected to electrophoresis were cut out and dissolved in water. The band immediately behind the leading one was

completely quenched by calcium. This indicated that the highly purified compound would give a very sharp end-point in the titration of calcium with EDTA.

*Fluorimetric Studies.*—*o*-Dianisidine-, *o*-diphenetidine-, and 3,3′-di(carboxymethoxy)-benzidine-*NNN′N′*-tetra-acetic acid showed maximum fluorescence at pH 5·5—6·0. The intensity of the fluorescence given by the other complexans was not sufficient for measurements to be undertaken with the available equipment except in the case of 3,3′-dicarboxybenzidine-*NNN′N′*-tetra-acetic acid. This substance showed slightly more fluorescence in sodium hydroxide and diethylamine solutions than in a buffer solution of pH 10.

## Experimental

*Preparation of* o-*Dianisidine*-NNN′N′-*tetra-acetic Acid* (*Tetrasodium Salt*).—*o*-Dianisidine (24·4 g.) was suspended in water (*ca.* 100 ml.) containing a small amount of phenolphthalein, in a 700-ml. round-bottomed flask fitted with a stirrer and two separatory funnels. The whole was placed on a steam-bath. A solution of sodium chloroacetate (49 g.) in water (100 ml.) was added dropwise from one funnel and 2N-sodium carbonate from the other in order to maintain the mixture at pH 8·0 corresponding to the colour of phenolphthalein. When all the sodium chloroacetate solution had been added, the reaction was allowed to proceed until further additions of sodium carbonate solution were unnecessary. The mixture was filtered to remove any unchanged diamine, and a concentrated solution of barium chloride was added until precipitation was complete. The mixture was warmed for about 30 min. on a steam-bath and barium *o*-dianisidine-*NNN′N′*-tetra-acetate was filtered off, washed with water, and dried under a vacuum (yield 80 g.). The barium content was determined by sulphate ashing (0·3293 g. gave 0·1969 g. of barium sulphate. Theor., 0·2058 g. for a dibarium salt). The barium salt was suspended in water and the required amount of sodium sulphate in solution was added. The mixture was stirred and warmed on a steam-bath for about 1 hr. and the precipitate of barium sulphate was filtered off. Ethanol was slowly added to the filtrate until precipitation was complete. The white precipitate was filtered off, washed with a little ethanol, and dried under a vacuum. The yield of white powder was 46·3 g. (32%).

The crude sodium salt (30 g.) was dissolved in sufficient water and boiled for a short time with charcoal. The filtrate from this treatment was diluted slowly with ethanol until precipitation just occurred. This precipitate was filtered off and rejected, and a large excess of ethanol was added to the filtrate. The white precipitate which was formed on stirring was filtered off, washed with a small amount of ethanol, and vacuum-dried (yield, 12 g.) (Found: Equiv., by non-aqueous titrimetry, 145; Na, from sulphated ash, 15·8%).

This product was considered sufficiently pure for use in the analytical studies of its properties as an indicator. Ultimate analysis gave results about 2% low for carbon, indicating the probable presence of inorganic salts as impurities. A purer product was obtained by suspending the sodium salt (10 g.) in ethanol (50 ml.) and cooling the suspension in salt–ice. A slow stream of hydrogen chloride was passed into the suspension until conversion of the sodium salt into the free acid was judged to be complete. The precipitated sodium chloride was filtered off and the filtrate was concentrated to half its bulk under reduced pressure. This solution was again filtered to remove a further small quantity of sodium chloride, and then poured into a fresh solution of sodium ethoxide (2 g. of sodium in 100 ml. of ethanol). The white, highly hygroscopic precipitate was filtered off, washed with ethanol, and vacuum-dried. On exposure to air, it rapidly absorbed moisture and slowly changed to a stable, dry white solid (Found: C, 44·0; H, 4·3; N, 4·8. Calc. for $C_{22}H_{20}Na_4N_2O_{10}$: C, 47·1; H, 3·6; N, 5·0. Calc. for $C_{22}H_{20}Na_4N_2O_{10},2H_2O$: C, 44·0; H, 4·1; N, 4·7%). An equivalent-weight determination by non-aqueous titrimetry gave a value of 148 (Calc. for the dihydrate, 150). The sodium content determined from the sulphated ash was 15·5% (Calc. for the dihydrate, 15·3%). These results indicate that the dihydrate is the normal product obtained when the tetrasodium salt is precipitated from aqueous solution by ethanol.

The other complexan salts were prepared similarly, the following yields being obtained, before final purification by fractional precipitation, from the corresponding benzidine derivatives: benzidine, 47%; *o*-diphenetidine, 29%; *o*-tolidine, 59%; 3,3′-di(carboxy-methoxy)benzidine, 59%; 3,3′-dicarboxybenzidine, 17%; 3,3′-disulphobenzidine, 25%

Only *o*-diphenetidine complexan was further purified *via* the free acid, the anhydrous tetrasodium salt forming a *dihydrate* on exposure to moist air (Found: C, 46·0; H, 3·7; N, 4·7. $C_{34}H_{34}Na_4N_2O_{10}.2H_2O$ requires C, 45·9; H, 3·9; N, 4·5%). The sodium salt of 3,3′-dicarboxybenzidine-*NNN′N′*-tetra-acetic acid could not be purified in this way because of the rapid decomposition of the free acid in the presence of hydrogen chloride. It and the remaining complexan salts were assayed by non-aqueous titrimetry and by determination of sulphated ash.

*Titration of Metal Ions with* EDTA.—The apparatus used is described by Belcher and Nutten.[4] The ultraviolet source was a Mazda mercury vapour electric discharge lamp of type MBW/U, 230—240 v, 125 w.

An intimate mixture of the sodium salt of the complexan and sodium chloride in the ratio of 1 : 100 was used as indicator.

*Procedure.* The 0·02M-cation solution (10 ml.) in a 250 ml. conical flask was diluted with about 50 ml. of water. Sufficient of an appropriate buffer solution and of the solid indicator mixture (5—10 mg.) was added. The titration was carried out in a darkened room with the solution in the titration vessel exposed to the source of ultraviolet light. The solution was titrated with EDTA (0·02M) to the appearance of fluorescence.

*Electrophoresis.* The apparatus and procedure previously described [2b] were used.

We are indebted to Cassella Farbwerke for a sample of *o*-diphenetidine, to Farbenfabriken-Bayer for a sample of benzidine-3,3′-disulphonic acid, and the Clayton Aniline Co. Ltd., for samples of benzidine-3,3′-di(oxyacetic acid) and 3,3′-dihydroxybenzidine. One of us (D. I. R.) thanks Messrs. J. Lyons & Co. for the award of a Fellowship.

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EDGBASTON, BIRMINGHAM 15. [*Received, December 28th*, 1960.]

[4] Belcher and Nutten, "Quantitative Inorganic Analysis," 2nd edn., Butterworths Scientific Publ., London, p. 174.

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## 1012. *The Spectra of Inorganic Complexes in Non-aqueous Solvents. Part I. Chlorocobaltate Ion and Cobalt Chloride.*

By S. BUFFAGNI and T. M. DUNN.

The spectra of $CoCl_2$ and the $[CoCl_4]^{2-}$ ion have been examined in various non-aqueous solvents, particularly nitromethane and *NN*-dimethylformamide. The results show that there is a considerable amount of interaction between the "solute" and the "solvent" and that species postulated as $[CoCl_3S_2]$, $[CoCl_3S]^-$, $[CoS_6]^{2+}$, and $[CoS_5Cl]^+$ occur in varying, but appreciable, amounts.

*NN*-DIMETHYLFORMAMIDE (DMF), dimethylacetamide (DMA), dimethyl sulphoxide (DMS), formamide, nitromethane (NM), and similar substances are frequently used as solvents for both organic and inorganic compounds; in particular, the first four are optically "transparent" to about 2800 Å when pure and can thus be used for spectroscopic purposes. The extent to which these solvents react with the solute has been underestimated in the past, especially with respect to inorganic complexes. In view of their increasing use, in both kinetics and spectroscopy, it seemed desirable to examine the spectrum of some well-characterised species and, for reasons which will be discussed by one of us elsewhere, the essentially tetrahedral cobalt halides were chosen for the study, the chloride ion $[CoCl_4]^{2-}$ being studied in detail.

Crystallographically authentic samples of this ion are now obtainable in the solid state combined with one of three different cations, as $Cs_3CoCl_5$,[1,2] $Cs_2CoCl_4$,[2] $[Et_4N]_2[CoCl_4]$,[3] and $[Ph_3MeAs]_2[CoCl_4]$.[4] The last two, being more soluble in organic solvents, have been

[1] Powell and Wells, *J.*, 1935, 359.
[2] Porai-Koshits, *Kristallografiya*, 1956, **1**, 291.
[3] Gill and Nyholm, *J.*, 1959, 3997.
[4] Gill, Nyholm, and Pauling, *Nature*, 1958, **182**, 168.

XUM

used to the largest extent in this investigation, but the cæsium salts have been used for single-crystal absorption and diffuse reflectance spectra of the solids since their crystallography is known more accurately.[2]

The visible spectra of the chlorocobaltate ion and of cobalt chloride have been extensively investigated in aqueous [5,6] and alcoholic solutions,[7,8] some non-hydroxylic solvents,[8] and nitromethane.[3] Re-examination of the spectrum in purified and dried nitromethane showed [9] that the solutions gave small but consistent departures from Beer's law and that the apparent maximum molar extinction coefficient of the solute was raised from the quoted values of 653 in nitromethane [3] and 603 in water [5a] by saturation of the

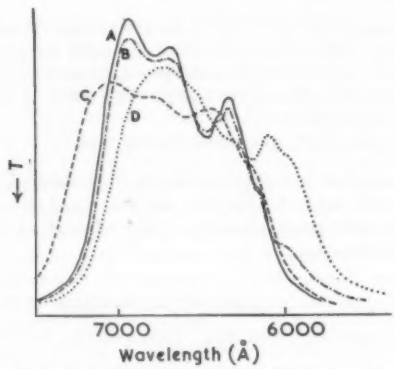


FIG. 1. Absorption spectra of (A) $[CoCl_4]^{2-}$ in nitromethane containing 0·1M-$Ph_3MeAsCl$, (B) $[CoCl_4]^{2-}$ in nitromethane solution, (C) Diffuse reflectance spectrum of $Cs_3CoCl_5$, and (D) $[CoCl_4]^{2-}$ in dimethylformamide.

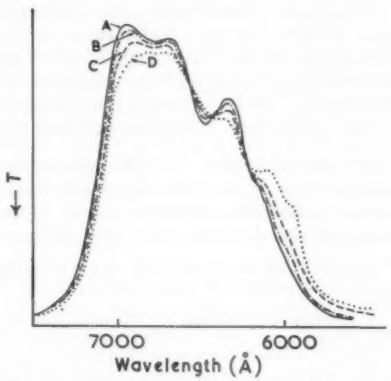


FIG. 2. $[CoCl_4]^{2-}$ in solution in 4 : 1 nitromethane–dimethylformamide, containing added chloride of concentrations (A) 0·2, (B) 0·4, (C) 0·6, and (D) $0·6 \times 10^{-3}$M.

solutions with chloride ion. The chloride was introduced as tetramethyl- or tetraethylammonium or methyltriphenylarsonium chloride, inorganic halides (*e.g.*, LiCl) being avoided on account of their known tendency to form ion pairs in non-aqueous solvents.[6] Also, since the methyltriphenylarsonium salt is not easily obtainable in large quantities and because it is easier to dry the tetramethylammonium salt to the degree required, most of the work was carried out with this. The tetramethylammonium salt has the disadvantage that its solubility is much lower (about 100 times) than that of its tetraethyl analogue or methyltriphenylarsonium salt, but this is not of importance except in studies at high chloride concentrations, where indeed the other salts were used.

In nitromethane the increase in molar extinction coefficient is accompanied by the disappearance of a weak band at 5940 Å and the more intense features of the spectrum of $[CoCl_4]^{2-}$ in nitromethane are finally obtained [9] as shown in Fig. 1A. (Fig. 1B shows the spectrum before chloride addition.) Comparison with the diffuse reflectance spectrum of $Cs_3CoCl_5$ given in Fig. 1C confirms the supposition that the spectrum obtained in the presence of excess of chloride ion is the spectrum of the authentic $[CoCl_4]^{2-}$ ion. Since, as

[5] (*a*) Kiss and Gerendas, *Z. phys. Chem.*, 1937, *A*, **180**, 117; (*b*) Dreisch and Trommer, *ibid.*, 1937, *B*, **37**, 37; Robinson and Brown, *Trans. Proc. Roy. Soc.* (*N.Z.*), 1948, **77**, 1; Katzin, *J. Amer. Chem. Soc.*, 1954, **76**, 3089.

[6] Smithson and Williams, *J.*, 1958, 457.

[7] Libus, Ugniewska, and Minc, *Roczniki Chem.*, 1960, **34**, 29; Barbinok, *J. Phys. Chem.* (*U.S.S.R.*), 1948, **22**, 1100.

[8] Katzin and Gebert, *J. Chem. Soc. Amer.*, 1950, **72**, 5464.

[9] Buffagni and Dunn, *Nature*, 1960, **188**, 937.

XUM

will be reported elsewhere, the diffuse reflectance curve is the same as the single-crystal absorption spectrum of $Cs_3CoCl_5$ and, in addition, the spectrum in chloride-saturated nitromethane is independent of the nature of the cation and obeys Beer's law over a concentration range of 50 (from $0{\cdot}5 \times 10^{-4}$M to $2{\cdot}5 \times 10^{-3}$M), the spectrum in Fig. 1A is undoubtedly that of $[CoCl]_4]^{2-}$.

In dimethylformamide solution the spectrum is very different and is given in Fig. 1D for absence of chloride; the spectrum in the presence of chloride assumes the contour of Fig. 1A but with rather different $\varepsilon_{max.}$ values. Similar spectra have previously been obtained by Katzin and Gebert [8] for solutions of cobalt chloride in some organic solvents, such as benzene, quinoline, and chloroform. The $\varepsilon_{max.}$ values obtained for nitromethane and dimethylformamide solutions seem to depend only on the solubility limit of the arsonium chloride $Ph_3MeAsCl$ which, being more soluble than either of the ammonium salts, yields the highest value. The values obtained are given in the Table, and it must be emphasized that they are not necessarily the usual *molar* extinction coefficients since,

| | Peak 1 | | Peak 2 | | Peak 3 | | Peak 4 | |
|---|---|---|---|---|---|---|---|---|
| Solvent | $\lambda_{max.}$ | $\varepsilon$ | $\lambda_{max.}$ | $\varepsilon$ | $\lambda_{max.}$ | $\varepsilon$ | $\lambda_{max.}$ | $\varepsilon$ |
| NM | 6940 | 622 | 6690 | 555 | 6350 | 418 | 5950 | 100 |
| NM + $Me_4NCl$ | 6950 | 705 | 6680 | 606 | 6340 | 440 | | |
| NM + $Ph_3MeAsCl$ | 6950 | 750 | 6680 | 630 | 6340 | 465 | 6150s | 200 |
| DMF | 6780 | 490 | | | 6100 | 295 | | |
| DMF + $Me_4NCl$ | 6890 | 600 | 6740 | 590 | 6350 | 392 | 6120 | 282 |
| DMF + $Ph_3MeAsCl$ | 6950 | 820 | 6680 | 688 | 6350 | 513 | 6150s | 215 |
| $H_2O$ + 12M-HCl | 6970 | 620 | 6625 | 576 | 6233 | 385 | | |

as will be seen below, not all the absorption arises from a single absorbing species. For this reason, all the figures have been presented with an arbitrary ordinate of percent transmission $T$. Also, the solutions do not obey Beer's law in the absence of chloride and the values in the Table are for 1 cm. of solution having an optical density about 0·3, *i.e.*, 50% transmission.

The $\varepsilon$ values have been calculated on the basis that all the absorption is caused by a single species, and so the concentration of cobalt ion is the only value used. These "effective" extinction coefficients are useful since many of the spectra of the different species are superposed, making it impossible to disentangle them completely. A Beer's law check on the solutions of $[CoCl_4]^{2-}$ ions in dimethylformamide in the absence of added chloride shows a decrease of about 15% in $\varepsilon$ on ten-fold dilution over the concentration range $10^{-4}$ to $10^{-5}$M, so that it is clear that the solvent is involved in some rôle other than that of "passive" solvation. To ascertain the nature of the species present in the solutions, various procedures have been used and these will be discussed in turn.

(a) *Addition of Chloride Ion to a Solution of* $[CoCl_4]^{2-}$ *Ion.*—The solutions of $[CoCl_4]^{2-}$ ion in nitromethane and dimethylformamide have been studied spectrophotometrically over the range 8000—3500 Å at varying chloride concentrations. The method of continuous variations was not used since it can lead to incorrect conclusions, as has been pointed out by Libus, Ugniewska, and Minc.[7] Since the spectrum in dimethylformamide is different from that in nitromethane at low chloride concentrations ($\sim 10^{-2}$M), dimethylformamide was added to the chloride-saturated nitromethane solution to observe the interconversion. No change was found up to 30% of added dimethylformamide and above this limit there was a gradual change to the spectrum observed in pure dimethylformamide. The effect of changing the chloride concentration is, however, much more drastic and is used here to illustrate the differences between, as well as the interconversion of, the two species. A solution of $[CoCl_4]^{2-}$ ion in 4 : 1 nitromethane–dimethylformamide shows three isosbestic points as the chloride concentration is varied and this is illustrated in Fig. 2. Small amounts of water were also added: spectra taken during 48 hours then showed only a very small instantaneous decrease in $\varepsilon$ of the tetrahedral species with no important changes with time. In fact, if cobalt chloride hexahydrate is dissolved in

dimethylformamide directly,[10] the solution is blue and contains about 30% of tetrahedral species. From what follows it is clear that any added water forms a small amount of octahedral complex of the type $[Co(H_2O)_x(DMF)_yCl]$ and/or $[Co(H_2O)_p(DMF)_qCl_2]$ where $x + y = 5$ and $p + q = 4$.

The presence of three isosbestic points proves that essentially only two species are present. One of these has been identified beyond doubt as $[CoCl_4]^{2-}$. It is postulated that the other is $[CoCl_3(DMF)]^-$ on grounds of previous work,[8] and of probability, and from other evidence which follows. Conductivities have yielded no unambiguous information as to the nature of the species present since the solutions are never obtained with, beyond doubt, only two interconverting ions.

(b) *Addition of Chloride Ion to the Complex* $[Co(DMF)_6][ClO_4]_2$.—When a $[CoCl_4]^{2-}$ salt is dissolved in dimethylformamide, a weak band appears at about 5300 Å which is usually associated with an octahedral species. This band disappears when chloride is added to the solution, the octahedral being transformed into a tetrahedral form. In an endeavour to examine this equilibrium, the complex $[Co(DMF)_6][ClO_4]_2$ was prepared;

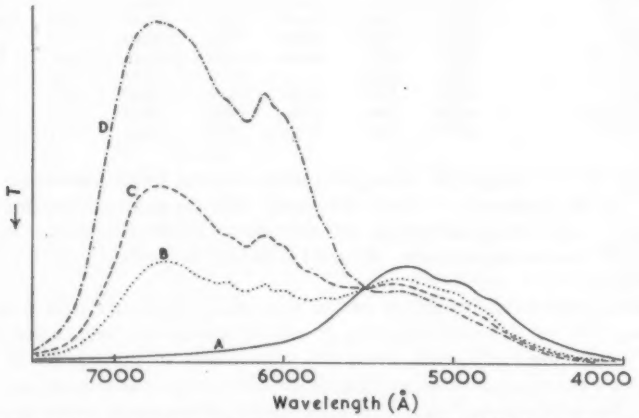


FIG. 3. Absorption spectrum of $4{\cdot}4 \times 10^{-3}$M-$[Co(DMF)_6][ClO_4)_2$ in 9 : 1 dimethylformamide–nitromethane containing added chloride of concentrations (A) 0, (B) 1·2, (C) 1·8, and (D) $4{\cdot}2 \times 10^{-3}$M.

its solution in dimethylformamide has a single broad band, with some structure, and a maximum at 5250 Å ($\varepsilon$ 21) (Fig. 3A). Curves 3B—D show the effect of added chloride ion, the final species being $[CoCl_4]^{2-}$ (not shown in Fig. 3). A finely graded series of spectra with respect to changing chloride concentration shows that in the Cl : Co range from 0 : 1 up to 7 : 1, the species previously postulated as $[CoCl_3(DMF)]^-$ exists in equilibrium with the octahedral complex, as shown by the presence of an isosbestic point. For ratios $\geqslant 8 : 1$ the same isosbestic points as are shown in Fig. 2 again appear, corresponding finally to conversion into $[CoCl_4]^{2-}$. In fact, there is never 100% conversion into $[CoCl_4]^{2-}$ in dimethylformamide when fully saturated tetramethylammonium chloride solutions are used, and it is not certain whether complete conversion is obtained even in the saturated solutions of the more soluble chlorides. The spectra overlap considerably and an exact estimate of the amounts of the individual species present cannot be made.

It seems certain also that more than one octahedral species is present at low Cl : Co ratios, since there are small but consistent shifts of the octahedral band maximum on the

[10] Pflaum and Popov, *Analyt. Chim. Acta*, 1955, **13**, 165; Dunn, Proc. Internat. Conf. Spectroscopy, Bologna, 1959, in the press.

addition of chloride. One additional species is certainly formed, and perhaps also a second. By analogy with the behaviour of $[Mn(H_2O)_6](ClO_4)_2$ on addition of chloride,[11] it is assumed that the second species is $[Co(DMF)_5Cl]^+$, the doubtful one being $[Co(DMF)_4Cl_2]$. The isosbestic point is not much affected by this multiplicity of octahedral species since the extinction coefficient at the crossing point is almost identical for both (or all) of them. There are, however, small departures from a strict " point " crossing which confirm the presence of more than two interconverting species (this is also true of the tetrahedral form—see below).

At the highest chloride concentrations attainable with the methylammonium salt, it is found that the dimethylformamide solutions obey Beer's law to within experimental error over a dilution range from $10^{-3}$ to $5 \times 10^{-5}$M, chloride-saturated dimethylformamide being the diluent; and the ratios of the individual peak heights also remain constant within experimental error. Unfortunately it is not possible to determine the equilibrium constants of the various reactions taking place during the octahedral–tetrahedral conversion since, apart from activity considerations,[6] up to a Cl : Co ratio of about 8 : 1 there are probably five species present, namely, $[CoCl_4]^{2-}$, $[CoCl_3(DMF)]^-$, $[Co(DMF)_4Cl_2]$, $[Co(DMF)_5Cl]^+$, and $[Co(DMF)_6]^{2+}$. If the presence of $[Co(DMF)_4Cl_2]$ is ignored, analysis of the results shows that at the concentration represented by curve 3C (*i.e.*, a Cl : Co ratio of 0·27 : 1) the solution contains $[Co(DMF)_6]^{2+}$ 72%, $[Co(DMF)_5Cl]^+$ 21%, $[CoCl_3(DMF)]^-$ 6·5%, and $[CoCl_4]^{2-}$ 0·5%. The analysis holds good below Cl : Co ratios of about 0·5 : 1, but above this value there seems to be a change in mechanism of formation and the concentration of $[CoCl_4]^{2-}$ rises quickly with respect to that of $[CoCl_3(DMF)]^-$ and there is also a change in the ratio of $(Co(DMF)_6]^{2+}$ to $[Co(DMF)_5Cl]^+$. The set of equilibria is now being studied in much more detail.

(c) *Addition of Chloride Ion to Solutions of Anhydrous Cobalt Chloride.*—Anhydrous cobalt chloride was dissolved severally in nitromethane and dimethylformamide in an endeavour to confirm the nature of the species postulated above.

(i) *Nitromethane solution.* The spectra obtained can be explained on the basis of the following equilibria:

$$CoCl_2 + NM \rightleftharpoons [CoCl_2(NM)_2]$$

$$[CoCl_2(NM)_2] + Cl^- \rightleftharpoons [CoCl_3(NM)]^- + NM$$

$$[CoCl_3(NM)]^- + Cl^- \rightleftharpoons [CoCl_4]^{2-} + NM$$

Experimentally, three distinct spectra (Fig. 4) were observed depending on the concentration of added chloride. Curve 4A is obtained only when the nitromethane and cobalt chloride are dried to the practical limit and addition of chloride, or water in small amounts, converts it into 4B, which is then converted into 4C by further addition of chloride. It is clear that curve 4C is the spectrum of $[CoCl_4]^{2-}$ and 4B is that of the species which occurs when $[CoCl_4]^{2-}$ is simply dissolved in pure dry nitromethane (see Fig. 1B). The species giving rise to curve 4B is here formulated as $[CoCl_3(NM)]^-$, and that giving rise to 4A as $[CoCl_2(NM)_2]$. The latter assignment is supported by the fact that this solute is a non-electrolyte. No evidence of an octahedral species was found in these dry solutions, although it was carefully looked for. There does not seem, therefore, to be an equilibrium of the octahedral–tetrahedral type in a solution of cobalt chloride in nitromethane and this possibly explains the appearance of the $[CoCl_2(NM)_2]$ which has no analogue in the dimethylformamide solution (see below). In view of the *a priori* possibility [12] of the loss of $Cl^-$ from cobalt chloride the solution was examined for traces of chloride down to about $10^{-5}$M; that none was found seems to eliminate the possibility that the *aci*-nitromethane negative ion is the co-ordinating species rather than nitromethane itself. The true molar extinction coefficient of the $[CoCl_3(NM)]^-$ species lies in the range 300—400 and that of

[11] Schlafer, *Z. phys. Chem.*, 1956, **6**, 201; Jörgensen, *Acta Chem. Scand.*, 1957, **11**, 53.
[12] Pocker, *J.*, 1958, 240.

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$[CoCl_3(NM)_2]$ in the range 65—75, but it is difficult to determine them with certainty, since there is always enough water present in the solutions to allow some " disproportionation " of $[CoCl_2(NM)_2]$ into $[CoCl_4]^{2-}$ and $[CoCl_3(NM)]^-$, with probably some $[Co(H_2O)_5Cl]^+$ or $[Co(H_2O)_6]^{2+}$. Again, however, the concentration of these octahedral species is too small to be detected spectroscopically since the total cobalt concentration of the solution is only about $10^{-3}$M.

(ii) *Dimethylformamide solution.* The situation here is somewhat different from that of nitromethane solutions, and the spectra can be explained on the basis of the equilibria:

$$2CoCl_3 + DMF \rightleftharpoons [CoCl_4]^{2-} + [Co(DMF)_6]^{2+}$$

$$[CoCl_4]^{2-} + DMF \rightleftharpoons [CoCl_3(DMF)]^- + Cl^-$$

$$[Co(DMF)_6]^{2+} + Cl^- \rightleftharpoons [Co(DMF)_5Cl]^+ + DMF$$

Both in the presence and in the absence of extra chloride, only two tetrahedral species need be postulated to explain the spectra, *viz.*, $[CoCl_4]^{2-}$ and $[CoCl_3(DMF)]^-$, the former

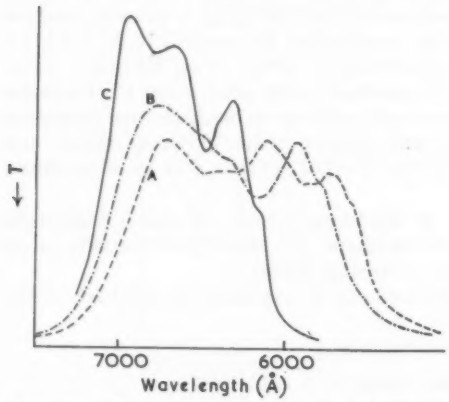


FIG. 4. Absorption spectrum of anhydrous cobalt chloride in dry nitromethane. (A) No added chloride; (B) $10^{-4}$M in chloride, $10^{-4}$-M in $Me_4NCl$; (C) $10^{-2}$M in chloride.

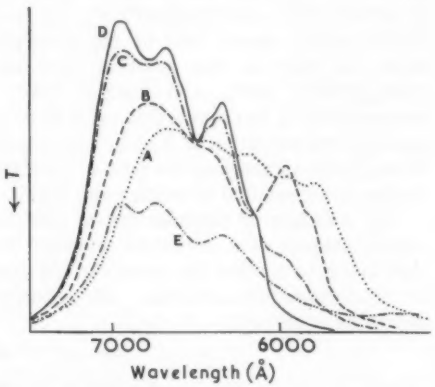


FIG. 5. Absorption spectra of $CoCl_2(DMF)_2$ in dry nitromethane, containing added chloride in concentrations (A) 0, (B) $10^{-4}$, (C) $10^{-3}$, and (D) $10^{-2}$M. (E) Diffuse reflectance spectrum of solid $CoCl_2(DMF)_2$.

to an extent of about 15—20%. The tri- and the tetra-chloride are readily formed in dimethylformamide since the octahedral species discussed in section (*b*) are formed readily in dimethylformamide and, since the Cl : Co ratio is only 2 : 1, the spectrum obtained is similar to one of those given already in Fig. 3. The molar extinction coefficient of the $[CoCl_3(DMF)]^-$ species is not known with certainty, but seems to be about 350. This has been estimated by subtracting curves corresponding to known amounts of $[CoCl_4]^{2-}$ from the experimental curve and can be done more readily here than for nitromethane solutions since no other tetrahedral species corresponding to $[CoCl_2(NM)_2]$ has been found in quantity.

These subtractions were, in fact, done with the reference cell in a double-beam spectrophotometer containing various amounts of $[CoCl_4]^{2-}$ in a $Ph_3MeAsCl$-saturated dimethylformamide solution. The difference curve is plotted by the spectrophotometer and it is relatively easy to observe the cross-over point from too much $[CoCl_4]^{2-}$ to too little. Since the total cobalt concentration is known it is possible to find the amount locked in the octahedral forms, and the concentration of $[CoCl_3(DMF)]^-$ in the original solution can thus be determined. In this way it has been established that a solution of cobalt chloride in

dimethylformamide contains, approximately, $[CoCl_4]^{2-}$ 10%, $[CoCl_3(DMF)]^-$ 35%, and 55% of various octahedral species. It is interesting that these values allow exactly one chloride ion per octahedral species and so the predominant ion is probably $[Co(DMF)_5Cl]^+$, although some $[Co(DMF)_4Cl_2]$ and some $[Co(DMF)_6]^{2+}$ may be present.

(d) *Isolation of a "Tetrahedral" Cobalt Complex of* DMF *and* $Cl^-$.—A complex with the empirical formula $CoCl_2(DMF)_2$ has been isolated and its spectrum measured both in nitromethane and as a solid by diffuse reflectance. The two spectra are completely different and the original hope that the solid would be the analogue of $[CoCl_2(NM)_2]$ was vain.

The spectra in nitromethane solution are interesting and have been studied with respect to both chloride and dimethylformamide addition. The spectrum for nitromethane solution given in Fig. 5A and its similarity to that of the postulated species $[CoCl_2(NM)_2]$ and $[CoCl_3(NM)]^-$ in Figs. 4A and B should be noted. It is, however, slightly different and this cannot be due simply to its being a superposition of various amounts of these two species, since there are small differences in $\lambda_{max.}$, particularly in the longest wavelength band. The spectrum does not obey Beer's law and appears to be brought near that of $[CoCl_2(NM)_2]$ by changing the relative intensities and positions of its bands; it is therefore suggested that the original spectrum arises from either $[CoCl_2(DMF)_2]$ or $[CoCl_2(NM)(DMF)]$; it is clearly never free from large amounts of $[CoCl_3(NM)]^-$.

Addition of chloride (curves 5B—D) seems to give anomalous results in that the spectrum of the species $[CoCl_3(NM)]^-$ appears first, to be followed by that of $[CoCl_4]^{2-}$. It seems that the addition results in replacement of dimethylformamide in the complex by $Cl^-$. Addition of dimethylformamide in small amounts (<5%) to the original solution (without addition of $Cl^-$) does not produce marked changes, but merely depresses the short-wavelength bands and increases the intensity of the band in the region of 6800 Å. This is almost certainly due to formation of small amounts of $[CoCl_3(DMF)]^-$.

The diffuse reflectance spectrum of the solid $CoCl_2(DMF)_2$ is shown in curve 5E. It is not identical with any of the solution spectra but, because of its contour and position, it could be present up to 20% concentration without being observed. This spectrum shows marked similarities with that of $Cs_3CoCl_5$ (Fig. 1C) and, in addition, has a weak band at about 5250 Å which is where $[Co(DMF)_6]^{2+}$ absorbs. On these grounds, the complex has been formulated tentatively as $[Co_2Cl_6][Co(DMF)_6]$, *i.e.*, as containing a dimeric tetrahedral cobalt chloride anion.

(e) *Diffuse Reflectance Spectra.*—The diffuse reflectance spectra have been discussed briefly above but it is important to emphasize that the present work has confirmed the essential identity of the diffuse reflectance, Nujol mull, and single-crystal measurements on the salts $Cs_3CoCl_5$, $[Et_4N]_2[CoCl_4]$, and $[Ph_3MeAs]_2[CoCl_4]$. The contours are identical within experimental error, even though there are slight differences (~200 $cm.^{-1}$) in the wavelengths of the maxima obtained by the different methods. It is then difficult to understand the spectra of $[CoCl_4]^{2-}$ in bromide discs at −196° (see Katzin [5]), and some of the bands in the aqueous solution measurements [5a] (in 13N-hydrochloric acid). Since it seems that only about two-thirds of the cobalt is present as tetrachlorocobaltate under these conditions it might well be that some of the bands are caused by the species $[CoCl_3(H_2O)]^-$.

(f) *Spectra in Other Non-aqueous Solvents.*—The spectra of cobalt(II) chlorides have also been examined for solutions in dichloromethane, ligroin, tetramethylene sulphone, dimethylacetamide, dimethyl sulphoxide, and ethyl acetate. In all cases, except dichloromethane, a solution of $[Ph_3MeAs]_2[CoCl_4]$ has much the same spectrum as in dimethylformamide. The spectrum in dichloromethane is identical in contour with that of $[CoCl_4]^{2-}$ in nitromethane, although the $\varepsilon_{max.}$ value is 675 compared with 705 for tetramethylammonium chloride-saturated nitromethane solution. The dimethyl sulphoxide solution contains only a relatively small amount of tetrahedral species (~20%), and most of the solute is present as various octahedral forms; the spectra of these solutions are given in Fig. 6.

The order of the solvents with respect to preservation of the original tetrahedral species is $CH_2Cl_2 > NM > DMA > DMF > DMS > EtOAc$, and the lack of co-ordinating power of dichloromethane appears to suggest its use as a convenient solvent for inorganic spectroscopy.

The spectrum of anhydrous cobalt chloride in each of these solvents has also been obtained and, in most cases, the effects of added chloride observed. The curves for ligroin solution are shown in Fig. 7, since one of the many coincidences which are a feature of the tetrahedral cobalt solutions is here apparent. Thus the spectrum at lowest chloride concentration shows little evidence of $[CoCl_4]^{2-}$ (<10% must be present, as seen from the changing peak height of the 5850 Å band) and yet there are already three bands (those at

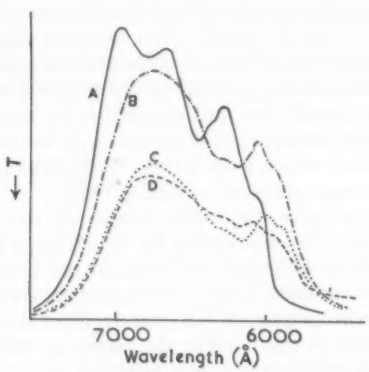


FIG. 6. Absorption spectrum of $[CoCl_4]^{2-}$ in (A) dichloromethane, (B) dimethylacetamide, (C) dimethylformamide, and (D) dimethyl sulphoxide.

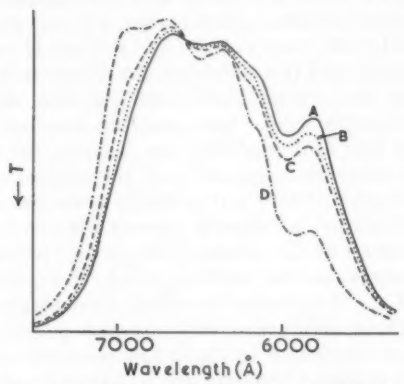


FIG. 7. Absorption spectrum of anhydrous cobalt chloride in ligroin solution containing 1% of dimethylformamide: (A) pure solvent; (B—D) added chloride, (B) $10^{-5}$M, (C) $10^{-4}$M, (D) $10^{-3}$M.

6680, 6400, and 6280 Å) which are common to both the initial and the final species (the presence of exceptionally sharp isosbestic points proves there to be only two species).

Of the other spectra it suffices to say that all have the contours of the various tetrahedral species $[CoCl_3S]^-$ (where S = solvent), thereby showing the capacity of the solvents to disproportionate the solute and to form octahedral and tetrahedral species. Only with ethyl acetate is it by no means clear that a tetrahedral species is involved, since the spectrum is sufficiently different to make it impossible to claim definitely a tetrahedral or a square planar form (or a badly distorted form between the two). The solubility of cobalt chloride in nitromethane is unfortunately too low to allow accurate magnetic moment measurements as a check on the assumption [13] that the species giving rise to the spectra is spin-free planar cobalt. The spectra obtained are not discussed individually since the general principles of their reactions with the solvent seem to be those discussed above.

*Conclusions.*—Three different spectra have been found for solutions of cobalt chloride in nitromethane, including those containing added chloride ion. The first of these species (see Fig. 4A) is a non-electrolyte, and this supports its formulation as $[CoCl_2(NM)_2]^0$. It retains some features of the $[CoCl_4]^{2-}$ spectrum, but it is not impossible for it to be badly distorted from a perfect tetrahedron towards a square shape, as are the copper tetrahalides.[14] The second species (see Fig. 4B) is very similar in spectrum to $[CoCl_4]^{2-}$, and it seems that its distortion is not much larger than that for $[CoCl_4]^{2-}$, although if the distance between

[13] Cotton and Holm, *J. Amer. Chem. Soc.*, 1960, **82**, 2979.
[14] Helmholz and Kruh, *J. Amer. Chem. Soc.*, 1952, **74**, 1176.

the 6800 and the 5940 Å peaks is taken as a measure of distortion, then it is more distorted than $[CoCl_4]^{2-}$ by somewhat less than 1000 cm.$^{-1}$ energetically. This second species is never obtained on its own, but always accompanied by $[CoCl_4]^{2-}$, estimated at 10—20%, so that it is not possible to get absolutely unique isosbestic points for its conversion into $[CoCl_4]^{2-}$. It seems likely, however, that, being intermediate between a non-electrolyte of formula $[CoCl_2(NM)_2]$ and the ion $(CoCl_4]^{2-}$, it is to be identified as $[CoCl_3(NM)]^-$.

As has been observed above, the same species appears when $[CoCl_4]^{2-}$ is dissolved in dry nitromethane and the suggested assignment thus appears highly probable. Conductivity data do not unambiguously assign the species as a mononegative ion, since there are at all times two other species present, one a non-electrolyte and the other doubly charged, and both are present in unknown amounts (since all three spectra overlap badly) so that the results are not definitive. Efforts to obtain the material as a solid have failed, but there seems little doubt as to its nature.

In a dimethylformamide solution of $[CoCl_4]^{2-}$ salts it can be shown that there is about 30% of $[CoCl_4]^{2-}$ present, together with some other species which it has been suggested

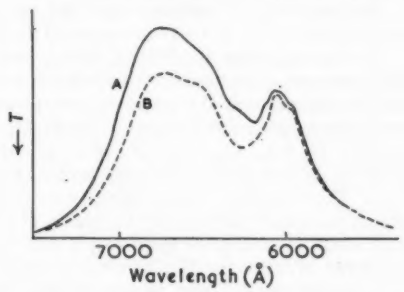


FIG. 8. (A) Absorption spectrum of $[CoCl_4]^{2-}$ in dimethylformamide solution. (B) The same curve after subtraction of that for 30% of $[CoCl_4]^{2-}$.

is $[CoCl_3(DMF)]^-$. The figure of 30% is reasonably certain, since a fair estimate of the true molar extinction coefficient has been obtained from experiments of the type described in sections (b) and (c). The coefficient is ~350, and curve 8A shows a solution of $[CoCl_4]^{2-}$ in dimethylformamide, while 8B is a curve obtained by subtracting 30% of $[CoCl_4]^{2-}$ from A. The latter curve bears a strong resemblance in contour to curve 4B for $[CoCl_3(NM)]^-$ and it seems safe to conclude that both of these species are of the type $[CoCl_3S]^-$. The similarity, and yet difference, between the nitromethane and dimethylformamide species provide evidence that the spectra observed in non-aqueous solvents are not due to a simple polymerisation or association of the solute (since the spectra would be the same in that case, apart from a small solvent shift). The value of the molar extinction coefficient for the species $[CoCl_2(NM)_2]$ is worthy of comment. The very low value found (65—75) strongly suggests a large distortion towards a square-planar shape or at least some species possessing a pseudo-centre of symmetry. Such square-planar forms have been postulated by Cotton and Holm,[13] and their spectra are not dissimilar to that given in Fig. 4A—Cotton and Holm's $\epsilon_{max.}$ are somewhat lower, but this is unimportant in view of the difficulty experienced in measuring this value and it should be taken as indicating only the correct magnitude.

All the spectra of solid $CoCl_2(DMF)_2$ in nitromethane solution can be explained in terms of superposition of varying amounts of the species $[CoCl_2(NM)(DMF)]$ and $[CoCl_2(NM)_2]$, together with $[CoCl_3(NM)]^-$, and justify confidence in the correctness of the assignments made.

It has not proved possible to obtain the equilibrium constants of the many equilibria involved, but it is hoped that this can be done by other methods. In addition, the equilibria of the tetrabromocobaltate ion and of the nickel tetrahalides have been examined and will be discussed elsewhere.

## Experimental

*Purification of Solvents.*—(a) *Nitromethane.* Two methods of preparing pure dried nitromethane were used since that using phosphorus pentoxide [12] was not suitable for spectroscopic work because of the fine suspended solid material present even after distillation. Nitromethane was refluxed with active charcoal for 24 hr., a current of oxygen-free nitrogen being bubbled through the liquid. The suspension was then filtered, dried ($Na_2SO_4$), and distilled, the fraction of b. p. 101—102°/760 mm. being collected. This was twice passed through an alumina column and redistilled. The method for the solvent used in conductivity measurements is that described by Pocker.[12] It was never found possible to obtain a water content below about 0·02% (~$10^{-2}$M).

(b) NN-*Dimethylformamide.* Benzene (5% by volume) was added to the solvent, and the azeotrope over the range about 85—120° collected and then distilled twice; the fraction boiling at 155·0—155·2°/760 mm. was redistilled at about 5 mm., the final solvent having b. p. 50—51°. It was stored out of contact with oxygen and tested with 1-fluoro-2,4-dinitrobenzene for traces of colour indicating the presence of free amine. The water content of these solutions was usually in the range 0·05% (~$2 \times 10^{-2}$M).

*Preparation of Complexes.*—(*a*) The tetrahedral cobalt complexes used were either kindly supplied by Dr. N. S. Gill [3] or prepared according to the literature.[3]

(*b*) The complex $[Co(DMF)_6](ClO_4)_2$ was prepared by stoicheiometric addition of silver perchlorate to a solution of anhydrous cobalt chloride in dimethylformamide. Silver chloride was filtered off and the complex precipitated by dried ether. The *complex* is a pale pink, very hygroscopic solid (Found: C, 31·4; H, 6·5; Cl, 10·2; N, 12·3. $C_{18}H_{42}Cl_2CoN_6O_{14}$ requires C, 31·0; H, 6·1; Cl, 10·2; N, 12·1%). The magnetic moment of the solid was determined at 297° K as 5·03 B.M., this being normal for an octahedral complex of the suggested type.

(*c*) The *complex* $CoCl_2(DMF)_2$ was precipitated from dimethylformamide solutions of anhydrous cobalt chloride by an excess of ether. It separates as a dark blue microcrystalline solid which is extremely hygroscopic and must be kept over $P_2O_5$ (Found: C, 27·0; H, 5·35; Cl, 26·25; N, 10·5. $C_6H_{14}Cl_2CoN_2O_2$ requires C, 26·1; H, 5·1; Cl, 25·7; N, 10·15%).

*Conductivities.*—These measurements were definitive only for nitromethane solutions. A saturated nitromethane solution of cobalt chloride at 20° gave a conductivity of $3{\cdot}20 \times 10^{-6}$ ohm$^{-1}$ cm.$^2$, compared with a value of $2{\cdot}03 \times 10^{-6}$ ohm$^{-1}$ cm.$^2$ for pure nitromethane (which rises to $2{\cdot}40 \times 10^{-6}$ ohm$^{-1}$ cm.$^2$ after 10 min.). These solutions are about $10^{-3}$M in $CoCl_2$, so that the molar conductance is about unity compared with about 100 for a uni-univalent electrolyte, 175—200 for a uni-bivalent electrolyte, and 250 for a uni-tervalent electrolyte.[3] The results confirm the non-electrolyte character of the solute.

The solutions were examined for traces of free hydrogen chloride by streaming a current of dry nitrogen through them, condensing any volatile material in a liquid-oxygen trap, and titrating the condensed liquid. Addition of hydrogen chloride to pure nitromethane showed that it could be detected in concentrations as low as about $10^{-5}$M. None was detected in the solution described above.

*Spectral Data.*—Solution spectra were done both with a Cary model [10] and a Unicam S.P. 500 instrument. The solid spectra were examined by using the Unicam diffuse reflectance apparatus attached to a normal Unicam S.P. 500 instrument.

*Anhydrous Chemicals.*—Anhydrous cobalt chloride was obtained by drying the hexahydrate at 130° for 4 hr. and allowing it to cool over $P_2O_5$. Methyltriphenylarsonium, tetraethylammonium, and tetramethylammonium chloride were dried under reduced pressure at 100°.

The authors acknowledge assistance by Dr. J. Parker who supplied the purification method for *NN*-dimethylformamide and by Mr. N. Daly as regards purification of nitromethane. Professor R. S. Nyholm, F.R.S., and Dr. J. Lewis are also thanked for many helpful discussions, also Mr. A. V. Winter for the accurate determination of the molar extinction coefficients. One of us (S. B.) acknowledges a grant from the Comitato Nazionale delle Richerche (C.N.R.) and the encouragement of Professor G. Peyronell of the Università di Modena.

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# 1013. *Thermochemical Studies. Part VI.*[1] *Heats and Entropies of Reaction of Transition-metal Ions with Triethylenetetramine.*

By L. Sacconi, P. Paoletti, and M. Ciampolini.

The heats of reaction of 3*d* bivalent metal ions with triethylenetetramine in 0·1M-potassium chloride at 25° have been measured calorimetrically. From these values and published values of free-energy changes the corresponding entropy changes have been calculated. The stabilities of these complexes are nearly equal to those of the corresponding bisethylenediamine complexes. This arises from a balance between their lower heats of formation and their higher entropy changes. The chelate effect for the replacement of ammonia by triethylenetetramine appears to be mainly due to the higher entropy of the ammonia molecules than that of triethylenetetramine. The heat of formation as well as the spectrum of the protonated ion [Cu Htrien]$^{3+}$ have been measured and compared with those of the analogous [Cu den]$^{2+}$ ion. The magnetic moment of [Co trien]$^{2+}$ was found to be 4·8 B.M., thus indicating a high-spin configuration.

In previous studies the heats of stepwise formation of the chelate complexes of bivalent transition ions from manganese to zinc with the bidentate ligand ethylenediamine[2] and the terdentate ligand diethylenetriamine[3] were measured. This research has now been extended to the tetradentate ligand triethylenetetramine (trien), $H_2N{\cdot}CH_2{\cdot}CH_2{\cdot}NH{\cdot}CH_2{\cdot}CH_2{\cdot}NH{\cdot}CH_2{\cdot}CH_2{\cdot}NH_2$. For this purpose direct calorimetric measurements of the heats of formation of the 1 : 1 complexes of this base with the above cations were carried out in 0·1M-potassium chloride and the results are reported in the present paper. Jonassen and his co-workers[4] have reported some values of the heat of formation of triethylenetetramine complexes calculated from the isobar equation. However, their values do not appear to be reliable, owing to the narrow temperature range of ten degrees investigated.

## Experimental

*Materials.*—Technical triethylenetetramine containing a large proportion of 2,2′,2″-triaminotriethylamine (tren) was purified by fractional crystallization of the hydrochlorides (tren,3HCl and trien,4HCl) from ethanol–water.[5] To the saturated solution of the pure triethylenetetramine hydrochloride a concentrated solution of sodium hydroxide was added, and the precipitate of sodium chloride filtered off and washed with ethanol. The solution of amine was concentrated and then distilled *in vacuo*. The triethylenetetramine was titrated potentiometrically against hydrochloric acid and proved to be 99·8% pure. It was dissolved in carbon dioxide-free 0·1M-potassium chloride and its concentration was determined potentiometrically against hydrochloric acid.

The preparation and standardization of the solutions of the different metal sulphates have already been described.[2] The nitrogen was purified by passage through copper gauze at 400°.

*Calorimetric Measurements.*—The calorimeter and the general procedure used were described in previous reports.[2,3] With manganese, iron, and cobalt, oxidation was avoided by bubbling a slow stream of nitrogen into the calorimetric solution. For each run the bottle was filled with *ca.* 24 ml. of a 0·4M-metal sulphate. A weighed amount of the base and, when necessary, of hydrochloric acid was placed in the Dewar flask and the volume made up to about 930 ml. with carbon dioxide-free 0·1M-potassium chloride. The final concentration of the metal complexes was about 0·01M.

The base was in slight excess (1—2%) on the 1 : 1 base–metal ratio. Under these conditions the metal ions were wholly present as [M trien]$^{2+}$ complexes. A larger excess of the base

[1] Part V, Ciampolini and Paoletti, *J. Phys. Chem.*, 1961, **65**, 1224.
[2] Ciampolini, Paoletti, and Sacconi, *J.*, 1960, 4553.
[3] Ciampolini, Paoletti, and Sacconi, *J.*, 1961, 2994.
[4] Jonassen, Hurst, LeBlanc, and Meibohm, *J. Phys. Chem.*, 1952, **56**, 16.
[5] Jonassen, LeBlanc, Meibohm, and Rogan, *J. Amer. Chem. Soc.*, 1950, **72**, 2430.

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was avoided in order to prevent the formation of the $[M_2 trien_3]^{4+}$ complexes.[4] For manganese, a 4—30% excess of the base was used. According to the values of the relevant stability constants, manganese is present as 97—99% of $[M trien]^{2+}$ and 3—1% of aquo-ion. In the calculations of the molar heat of reaction, allowance was made for the amount of unreacted manganese(II) ions.

The heat evolved was corrected for the thermal effect arising from the dissociation of the base in water.

For each metal–base system two independent sets of three runs were carried out with different solutions of the reactants.

In the experimental determination of the heat of formation of the $[Cu Htrien]^{3+}$ ion the distribution of the ionic species present in the various systems before and after the reaction was calculated by using the known values of the equilibrium constants determined in 0·1M-potassium chloride.[6] As these constants are given at 20°, they were corrected to 25° by using the values of $\Delta H$ obtained in this work, the method of successive approximations being employed.

TABLE 1.

The system $CuSO_4$ + HCl + trien in 0·1M-potassium chloride.

| Copper ($10^{-5}$ mole) | HCl ($10^{-5}$ mole) | trien ($10^{-5}$ mole) | $Q$ (cal.) | $Q_{cs}$ (cal.) | $-\Delta H$ (kcal. mole$^{-1}$) | |
|---|---|---|---|---|---|---|
| 983 | 1398 | 1145 | 152·4 | 16·8 | 15,860 | $\Delta G = -18{\cdot}80 \pm 0{\cdot}3$ (kcal. mole$^{-1}$) |
| 906 | 1291 | 1056 | 140·9 | 14·7 | 15,810 | $\Delta H = -15{\cdot}80 \pm 0{\cdot}1$ (kcal. mole$^{-1}$) |
| 891 | 4596 | 1790 | 78·7 | 54·7 | 15,680 | $\Delta S = 10{\cdot}0 \pm 1{\cdot}3$ (cal. deg.$^{-1}$ mole$^{-1}$) |
| 916 | 4723 | 1840 | 82·0 | 56·2 | 15,830 | |
| | | | | | Mean = 15,800. | |

TABLE 2.

Thermodynamic functions for metal(II)–triethylenetetramine systems in 0·1M-potassium chloride at 25°.

| | $Mn^{2+}$ | $Fe^{2+}$ | $Co^{2+}$ | $Ni^{2+}$ | $Cu^{2+}$ | $Zn^{2+}$ |
|---|---|---|---|---|---|---|
| $-\Delta G$ (kcal. mole$^{-1}$) [a] | 6·70 ± 0·07 | 10·50 ± 0·07 | 14·90 ± 0·14 | 18·80 ± 0·28 | 27·40 ± 0·14 | 16·40 ± 0·07 |
| $-\Delta H$ (kcal. mole$^{-1}$) [b] | 2·30 ± 0·05 | 6·05 ± 0·05 | 10·65 ± 0·15 | 14·00 ± 0·10 | 21·55 ± 0·10 | 8·90 ± 0·15 |
| $\Delta S$ (cal. deg.$^{-1}$ mole$^{-1}$) | 15·0 ± 0·5 | 15·0 ± 0·5 | 14·5 ± 1·0 | 16·0 ± 1·5 | 19·5 ± 1·0 | 25·0 ± 0·5 |

[a] Cf. ref. 6; corrected to 25° by using the enthalpy values obtained in this work. [b] Jonassen's values (ref. 4) for $-\Delta H$, in kcal. mole$^{-1}$, are: Mn 4; Fe 9; Co 9; Ni 13; Cu 22; Zn 4.

*Magnetic Measurements.*—The magnetic susceptibility of the solution of the $[Co trien]^{2+}$ ion was determined by using a Gouy-type magnetic balance.[7]

In order to prevent oxidation, the solution of the complex ion was prepared as follows. Weighed amounts of standardized solutions of cobalt(II) sulphate and triethylenetetramine in the molar ratio 1 : 1 were separately freed from dissolved oxygen by passage of nitrogen for 20 min. The two solutions were then mixed and stoppered. All the above operations were performed in an atmosphere of pure nitrogen.

The susceptibility of the $[Co trien]SO_4$ complex was determined according to the formula:

$$\chi_{g(complex)} = [\chi_{g(solution)} - (1 - x)\chi_{g(solvent)}]x^{-1}$$

where $x$ = fraction by weight of $[Co trien]SO_4$ in the solution. Diamagnetic corrections for the organic ligand were calculated from the Pascal constants.[8] The diamagnetic susceptibility of the sulphate ion was taken as $-40{\cdot}10^{-6}$.[9]

*Spectrophotometric Measurements.*—The spectra of the copper complexes were measured with a Beckman DU spectrophotometer with 1 cm. stoppered silica cells. With the diethylenetriamine–copper(II) complex, buffering at *ca.* pH 6·3 was necessary to avoid the formation of $[Cu den(OH)]^+$. The spectrum of $[Cu trien]^{2+}$ was recorded for a 1 : 1 solution of copper sulphate and triethylenetetramine.

[6] Schwarzenbach, *Helv. Chim. Acta*, 1950, **33**, 974.
[7] Sacconi, Cini, Ciampolini, and Maggio, *J. Amer. Chem. Soc.*, 1960, **82**, 3487.
[8] Cf. Selwood, "Magnetochemistry," Interscience Publ. Inc., New York, 1956, p. 92.
[9] Klemm, *Z. anorg. Chem.*, 1941, **246**, 347; cf. ref. 8, p. 78.

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The solutions used to measure the spectrum of the [Cu Htrien]$^{3+}$ ion were 10·00mM in copper sulphate, 46·80mM in hydrochloric acid, 19·44mM in triethylenetetramine (test solution); and 2·20mM in copper sulphate, 1·63mM in triethylenetetramine (control). The composition of the test solution, calculated from the equilibrium constants,[6] was: Cu Htrien$^{3+}$, 7·81; Cu trien$^{2+}$, 1·63; $Cu^{2+}$, 0·56; $H_3$trien$^{3+}$, 2·41; $H_4$trien$^{4+}$, 7·59; $H^+$, 1·50 mmoles $l.^{-1}$. The only cations contained in the control solutions were $Cu^{2+}$ and [Cu trien]$^{2+}$; their concentrations were the same as in the test solution. Another spectrum was recorded in a similar way for a solution of the composition: Cu Htrien$^{3+}$, 6·20; Cu trien$^{2+}$, 0·65; $Cu^{2+}$, 3·15; $H_3$trien$^{3+}$, 1·37; $H_4$trien$^{4+}$, 8·63; $H^+$, 3·00 mmoles $l.^{-1}$. The value of $\lambda_{max.}$ and the shape of the spectra were the same in both cases, only the height of the maximum differing by about 7%. The mean of the two spectra is recorded in Fig. 1. This procedure was followed as it is impossible to prepare a solution containing copper entirely as the [Cu Htrien]$^{3+}$ ion.

## Results

The calorimetric details for the formation of the [Cu Htrien]$^{3+}$ complex ion are recorded in Table 1. The heat ($Q$) evolved in each experiment was corrected for the heat of dilution of the metal salt. The heat effects ($Q_{cr}$) due to the change in the concentration of the various protonated forms of the base on complex formation were calculated by using the values of the heats of stepwise neutralization.[10] The thermodynamic functions for the formation of [Cu Htrien]$^{3+}$ ion are also recorded.

Table 2 reports the values for the thermodynamic functions $\Delta G$, $\Delta H$, and $\Delta S$ relative to the reaction between bivalent metal ions from manganese to zinc and triethylenetetramine

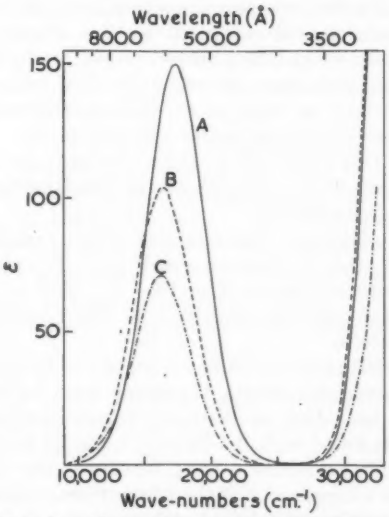



FIG. 1. Absorption spectra of complexes of copper and polyamines: A, [Cu trien]$^{2+}$; B, [Cu Htrien]$^{3+}$; C, [Cu den]$^{2+}$.

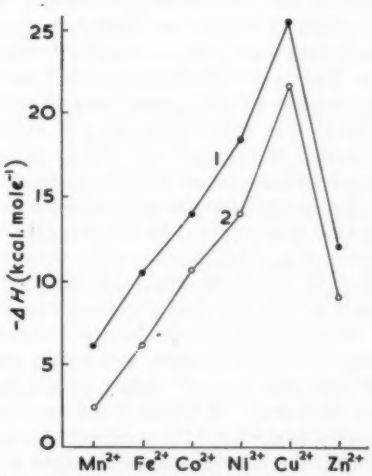



FIG. 2. Heats of formation of: (1) [M en$_2$]$^{2+}$ ions; (2) [M trien]$^{2+}$ ions.

in 0·1M-potassium chloride at 25°. The values of $\Delta G$ were obtained by using the stability constants of Schwarzenbach at 20°,[6] corrected at 25° by using our values of $\Delta H$.

The results of the magnetic measurements carried out at 24° were: $x = 5{\cdot}87 \times 10^{-3}$; $\chi_{g(solution)} = 1{\cdot}19 \times 10^{-6}$; $\chi_{g(complex)} = 31{\cdot}85 \times 10^{-6}$; $\chi_M = 9594 \times 10^{-6}$; $\delta = 151 \times 10^{-6}$; $\chi_{Co^{2+}} = 9745 \times 10^{-6}$; $\mu_{eff.} = 4{\cdot}83$ B.M.

The results of the spectrophotometric measurements are: [Cu trien]$^{2+}$, $\lambda_{max.} = 575$ mμ, $\varepsilon = 150$; [Cu den]$^{2+}$, $\lambda_{max.} = 610$ mμ, $\varepsilon = 71$; [Cu Htrien]$^{3+}$, $\lambda_{max.} = 610$ mμ, $\varepsilon = 104$. Fig. 2

[10] Our unpublished results.

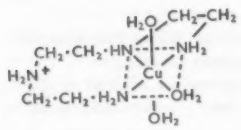
shows the absorption spectra of the $[Cu\ trien]^{2+}$, $[Cu\ den]^{2+}$ and $[Cu\ Htrien]^{3+}$ complex ions over the wavelength range 300—1000 mμ. The spectra of the first two complexes were already recorded for the ranges 430—670 [11] and 490—830 mμ [12] respectively.

## Discussion

The values of $\Delta H$, plotted against the atomic number of the metals in Fig. 2, increase monotonically from manganese to copper and then diminish to zinc for which the value falls between that of iron and cobalt. In this Figure the heats of formation of the $[M\ en_2]^{2+}$ complexes [2] are also shown. The fact that the two curves run parallel seems to indicate that the two series of complexes have the same structure, namely, diaquo-octahedral for the metals from manganese to copper and tetrahedral for zinc.[2] The heat changes for the $[M\ trien]^{2+}$ ions are 3—4 kcal. mole$^{-1}$ lower than for the corresponding $[M\ en_2]^{2+}$ complexes. An equal lowering was also found on going from $[M\ en_3]^{2+}$ to the corresponding $[M\ den_2]^{2+}$ complexes.[3] Both the $[M\ den_2]^{2+}$ and $[M\ trien]^{2+}$ complexes differ from the $[M\ en_3]^{2+}$ and $[M\ en_2]^{2+}$ complexes, respectively, in that they contain one chelate ring more and have two secondary nitrogen atoms in place of two primary ones. Both these factors probably lead to a lowering of the heat of reaction: the first as a result of the increased internal strain within the chelate rings; [13] the second as a result of the probable lower strength of the metal–secondary nitrogen bond as compared with the metal–primary one.[3] The latter hypothesis is supported by a comparison of the heats of formation of the $[Cu\ den]^{2+}$ and $[Cu\ Htrien]^{3+}$ complexes. The first complex ion which contains two primary and one secondary nitrogen atom bound to the copper(II) ion has a heat of formation of 18·00 kcal. mole$^{-1}$: [3] the second, in which the nitrogen donor atoms are one primary and two secondary,* has a heat of formation of only 15·80 kcal. mole$^{-1}$. This difference of 2·20 kcal. mole$^{-1}$ need not, in fact, be taken as the difference between the strength of the copper–primary nitrogen and copper–secondary nitrogen bonds. It is likely that some inductive and electrostatic effects as well as those arising from the hydration of the terminal $-NH_3^+$ group may affect the strength of the bond between copper and secondary nitrogen adjacent to the free chain.

No spectrophotometric evidence for the $[Cu\ Htrien]^{3+}$ complex ion, whose stability constant was reported by Schwarzenbach,[6] was found by Jonassen *et al.*[4] The absorption spectrum we obtained shows a maximum at 610 mμ (curve 2 in Fig. 1). This value differs by *ca.* 35 mμ from $\lambda_{max.}$ of $[Cu\ trien]^{2+}$ but coincides with $\lambda_{max.}$ of the $[Cu\ den]^{2+}$ which also has a group of three nitrogen donor atoms.

The entropy changes for the formation of triethylenetetramine complexes of bivalent manganese, iron, cobalt, and nickel ions are essentially constant, ranging from 14·5 to 16·0 cal. deg.$^{-1}$ mole$^{-1}$, while with copper and zinc they are distinctly higher than the preceding ones. A similar trend has already been found with the $[M\ en_2]^{2+}$ and $[M\ den]^{2+}$ complex ions,[2,3] and the same explanation probably holds here. Thus, for copper, the high value of the entropy can be ascribed to a planar arrangement of the triethylenetetramine molecule around the ion with a concomittant higher crystal field stabilization energy.[14] Thus the configuration of the $[Cu\ trien(H_2O)_2]^{2+}$ complex ion will mainly be *trans*-octahedral, while for the other metal ions from manganese to nickel the prevailing structure



* The other possible form (annexed) with an eight-membered ring is very improbable. It may be noted, in this connection, that the diamines tetramethylenediamine and hexamethylenediamine seem to act as non-chelating ligands.[13]

[11] Kirson, *Bull. Soc. chim. France*, 1957, 1178.
[12] Haendler, *J. Amer. Chem. Soc.*, 1942, **64**, 686.
[13] Schwarzenbach, *Helv. Chim. Acta*, 1952, **35**, 2344.
[14] Jørgensen, *Acta Chem. Scand.*, 1956, **10**, 887.

attributable to the complex ions on statistical and steric grounds [15] is *cis*-diaquaoctahedral. Since the dipole moment of the *trans*-octahedral structure is lower than that of the two possible *cis*-octahedral ones, the [Cu trien$(H_2O)_2$]$^{2+}$ ion will be able to orient fewer water molecules than the other ions, the entropy of the final state thus being higher.[16]

The value of $\Delta S$ for zinc, which is even higher than that for copper, leads to the hypothesis that more than four water molecules are released from the first co-ordination sphere of the aquo-ion with the consequent formation of a tetrahedral [Zn trien]$^{2+}$ ion. Such an ion, however, should have a larger second-sphere hydration since the spatial geometry should allow more water molecules to pack close to the metal ion. It may be noted, in this connection, that a tetrahedral structure was also postulated for other tri- and tetra-amine complexes of zinc.[2,3,17]

Let us now consider the displacement of ammonia and ethylenediamine respectively by triethylenetetramine:

$$[ML_n]^{2+} + \text{trien} \rightleftharpoons [M\ \text{trien}]^{2+} + nL \quad . \quad . \quad . \quad . \quad . \quad (1)$$

(L = $NH_3$ or en; $n = 4$ or 2). The corresponding functions are recorded in Table 3.

The enthalpy term for the replacement of ammonia by triethylenetetramine does not favour the formation of the [M trien]$^{2+}$ ions. The higher stability of these complexes arises from the larger value of the entropy term. Contrary to the free-energy and enthalpy changes, the entropy changes are roughly constant for every metal, but the results recorded in Table 3 are too scanty to allow definite conclusions to be drawn.

The chelate effect for the replacement of ethylenediamine by triethylenetetramine is negligible. In this case, too, the $\Delta H$ values do not favour the formation of the [M trien]$^{2+}$ complexes but this effect is compensated by the positive $\Delta S$ values.

The entropy changes accompanying the processes of type (1) may be expressed by the equation:

$$\Delta S = [\bar{S}^0(M\ \text{trien}) - \bar{S}^0(M\ L_n)] + [n\bar{S}^0(L) - \bar{S}^0(\text{trien})] \quad . \quad . \quad . \quad (2)$$

where the terms $\bar{S}^0$ indicate partial molal entropies. The values of $\bar{S}_0(NH_3)$ in water at 25° is 26·3 cal. deg.$^{-1}$ mole$^{-1}$.[18] No experimental values have been reported for the partial molal entropies of ethylenediamine and triethylenetetramine. The values, calculated according to the Cobble equation [19] are: $\bar{S}^0(\text{en}) = 44$; $\bar{S}^0(\text{trien}) = 84$ cal. deg.$^{-1}$ mole$^{-1}$. Then $[4\bar{S}^0(NH_3) - \bar{S}^0(\text{trien})] = 21 \pm 2$; $[2\bar{S}^0(\text{en}) - \bar{S}^0(\text{trien})] = 4 \pm 4$ cal. deg.$^{-1}$ mole$^{-1}$. . By substituting these values, together with the experimental values of $\Delta S$ in equation (2) we obtain:

$[\bar{S}^0(M\ \text{trien}) - \bar{S}^0(M(NH_3)_4)]$: Ni, 12; Cu, 14; Zn, 10 cal. deg.$^{-1}$ mole$^{-1}$,
$[\bar{S}^0(M\ \text{trien}) - \bar{S}^0(M\ \text{en}_2)]$: Mn, 8·5; Fe, 10·5; Co, 8·5; Ni, 9·0; Cu, 9·5; Zn, 10·5 cal. deg.$^{-1}$ mole$^{-1}$,

with an estimated uncertainty of $\pm 6$ cal. deg.$^{-1}$ mole$^{-1}$. These differences are positive and roughly constant. For the metathetic systems ethylenediamine–ammonia and trimethylenediamine–ammonia, Rasmussen [20] found values of these differences ranging from 0 to 8 cal. deg.$^{-1}$ mole$^{-1}$, with an indeterminacy of about $\pm 10$ cal. deg.$^{-1}$ mole$^{-1}$ and concluded that the entropy change is mainly due to the entropy difference between the ligands. For the triethylenetetramine–ammonia and triethylenetetramine–ethylenediamine systems the difference between the entropies of the complexes contributes in a

[15] Basolo, *J. Amer. Chem. Soc.*, 1948, **70**, 2634; Sarma and Bailar, *ibid.*, 1955, **77**, 5480.
[16] Chatt and Wilkins, *J.*, 1952, 4300; 1956, 525.
[17] Yatsimirskii and Milyukov, *Zhur. fiz. Khim.*, 1957, **31**, 842.
[18] National Bureau of Standards, "Selected Values of Chemical Thermodynamic Properties," Washington, D.C., Circular 500.
[19] Cobble, *J. Chem. Phys.*, 1953, **21**, 1446.
[20] Rasmussen, *Acta Chem. Scand.*, 1956, **10**, 1279.

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TABLE 3.

Thermodynamic functions for the replacements (1).

| | *n*L | $Mn^{2+}$ | $Fe^{2+}$ | $Co^{2+}$ | $Ni^{2+}$ | $Cu^{2+}$ | $Zn^{2+}$ |
|---|---|---|---|---|---|---|---|
| $\Delta G$ (kcal.) ..... | $4NH_3$ | | | | −7·85 | −10·00 | −3·35 |
| | 2en | −0·05 | −0·05 | −0·35 | 0·40 | −0·10 | −1·30 |
| $\Delta H$ (kcal.) ..... | $4NH_3$ | | | | 2·00 | 0·45 | 5·90 |
| | 2en | 3·70 | 4·35 | 3·30 | 4·35 | 3·85 | 3·00 |
| $\Delta S$ (cal. deg.$^{-1}$) ..... | $4NH_3$ | | | | 33·0 | 35·00 | 31·0 |
| | 2en | 12·5 | 14·5 | 12·5 | 13·0 | 13·5 | 14·5 |

comparable degree to the $\Delta S$ of replacement. When the replaced ligand is ammonia, the largest contribution to the entropy changes is given by the difference between the entropies of the ligands.

Concerning the stereochemistry of the complexes with triethylenetetramine, particular attention has been given to those of nickel(II) and cobalt(II). On the basis of magnetic measurements made on solutions of the [Ni trien]$^{2+}$ and [Co trien]$^{2+}$ ions, Jonassen *et al.*[21] stated that they are " low-spin " complexes. These workers have not, however, reported the values of either the magnetic susceptibility or, in the case of nickel, the ionic strength used. From spectrophotometric measurements on the [Ni trien]$^{2+}$ complex Jørgensen [22] showed that, at high temperature or strong salt concentrations, a yellow form, probably planar diamagnetic, does exist. Thus, under the conditions used for our calorimetric measurements, only a few percent of this form should occur. On the other hand, the magnetic moment of 4·8 B.M. we obtained for the triethylenetetramine–cobalt(II) complex in 0·2M-solution, indicates that this ion is " high spin."

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[21] Jonassen and Strickland, *J. Amer. Chem. Soc.*, 1958, **80**, 312; Jonassen and Ramanujam, *J. Phys. Chem.*, 1959, **63**, 411.
[22] Jørgensen, *Acta Chem. Scand.*, 1957, **11**, 399.

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## 1014. 2-*Amino*-2-*imidazolines and* 2-*Amino*-2-*oxazolines.*

By B. ADCOCK, ALEXANDER LAWSON, and D. H. MILES.

2-Amino-2-imidazoline has been prepared by the cyclisation of 2-guanidinoethylamine, which is produced in poor yield by the action of ethylenediamine on *S*-methylisothiouronium sulphate. A better general method for the preparation of 2-amino-2-imidazolines and 1,4,5,6-tetrahydropyrimidines is the action of cyanamide or dimethylcyanamide on the monotoluene-*p*-sulphonates of 1,2- or 1,3-diamines. The action of phenylcyanamide gives the 2-anilino-derivatives. Ethylenediamine with 2-amino-2-imidazoline gives a mixture of *N*-2-imidazolinyl- and *NN'*-di-2-imidazolinyl-ethylenediamine rather than the bicyclic 2,3,5,6-tetrahydro-1*H*-imidaz[1,2*a*]imidazole previously reported. 2-(Substituted amino)-2-oxazolines have been prepared from *N*-substituted *N'*-2-hydroxyethylthioureas by the action of methyl iodide and sodium ethoxide, and by thermal cyclisation of *NN'*-diphenylguanidinoethanols, which are prepared from diphenylcarbodi-imide and amino-alcohols.

2-AMINO-2-IMIDAZOLINE has been obtained as its salt by the action of cyanogen bromide on ethylenediamine,[1] and its substituted derivatives have been obtained by the action of

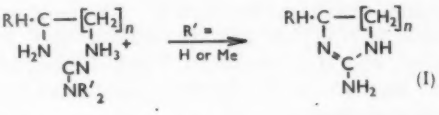
[1] Pierron, *Ann. Chim. Phys.*, 1919, **11**, 361.

amino-compounds on bromoethylcyanamides [2] or 2-methylthioimidazolines [3] or 2-nitroiminoimidazolidines.[4]

A possible synthetic route to 2-aminoimidazoline would be by ring closure of 2-guanidinoethylamine by loss of ammonia. This substance could not be obtained in appreciable quantity from cyanamide and ethylenediamine under various conditions, ethylenediguanidine being formed almost exclusively. A small yield of 2-aminoimidazoline, isolated as its picrate, was however obtained when the diamine reacted with methylisothiouronium sulphate at pH 7 and the intermediate monoguanidine sulphate was passed through Amberlite IRA-400 resin which effected ring closure.

A much better method of obtaining 2-aminoimidazolines was based on the procedure used for 2-substituted imidazolines by Oxley and Short [5] who heated cyanides with the monotoluene-*p*-sulphonate of ethylenediamine. This reaction has now been extended to include the use of cyanamide and substituted cyanamides.

When equimolecular amounts of ethylenediamine monotoluene-*p*-sulphonate and cyanamide are heated in the steam bath, ammonia is evolved and both ethylenediguanidine and 2-aminoimidazoline (I; R = H, $n = 1$) are formed as the toluene-*p*-sulphonates in about 20% yield. Use of dimethylcyanamide leads to dimethylamine formation and the




(I)

2-aminoimidazoline salt is readily isolated in about 50% yield. Either cyanamide or dimethylcyanamide (1 mol.) and trimethylenediamine (as monotoluene-*p*-sulphonate) similarly gave 2-amino-1,4,5,6-tetrahydropyrimidine (I; R = H, $n = 2$).

Benzimidazoles are readily formed from cyanamides and *o*-phenylenediamine, but, in the case of dimethylcyanamide, ammonia and not dimethylamine is evolved, the product being 2-dimethylaminobenzimidazole as confirmed by its preparation from 2-chlorobenzimidazole and dimethylamine.[6]

When phenylcyanamide reacts with ethylenediamine toluene-*p*-sulphonate, ammonia is slowly evolved, and from the product, consisting of both the diguanidino-derivative of ethylenediamine and the imidazoline, the latter can be isolated as picrate from which the free base is liberated. That this product is 2-anilino-2-imidazoline (II; R = H, $n = 1$) and not the 1-phenyl isomer, is proved by its preparation from 2-methylthioimidazoline by a modification of Aspinall and Bianco's method.[3] In the reaction between phenylcyanamide and trimethylenediamine toluene-*p*-sulphonate the corresponding 2-anilinotetrahydropyrimidine (II; R = H, $n = 2$) is produced.

Similar results were obtained with propylenediamine. With an equimolecular quantity of cyanamide or, better, with 2 mol. of dimethylcyanamide the toluene-*p*-sulphonate of 2-amino-4-methylimidazoline (I; R = Me, $n = 1$) is formed; the oily base gives a crystalline picrate and nitrate. When phenylcyanamide is used, the non-crystalline reaction product, after conversion into the picrate, yields the crystalline 4-methyl-2-anilinoimidazoline (II; R = Me, $n = 1$).

Pierron claimed [1] to have prepared the bicyclic 2,3,5,6-tetrahydro-1*H*-imidaz[1,2*a*]-imidazole (III) by heating 2-aminoimidazoline with an excess of ethylenediamine for 48 hr. He described a dipicrate, m. p. 203°, and a dihydrobromide, m. p. 224°. The product

[1] Elderfield and Hageman, *J. Org. Chem.*, 1949, **14**, 605; Elderfield and Green, *ibid.*, 1952, **17**, 442.
[2] Aspinall and Bianco, *J. Amer. Chem. Soc.*, 1951, **73**, 602; McKay and Hatton, *ibid.*, 1 56, **78**, 1618.
[4] McKay, Buchanan, and Grant, *J. Amer. Chem. Soc.*, 1949, **71**, 766.
[5] Oxley and Short, *J.*, 1947, 497.
[6] Efros, Porai-Koshits, and Farbenshtein, *Zhur. obshchei Khim.*, 1953, **23**, 1691.

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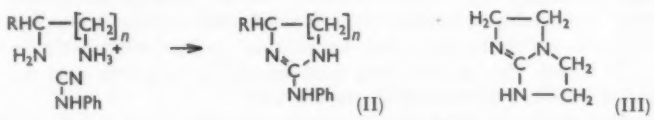
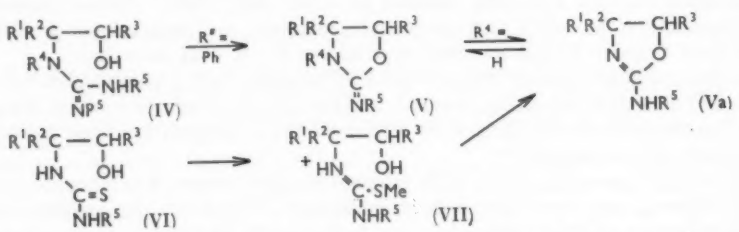
obtained by us under his conditions was converted into the picrate; fractional crystallisation gave two compounds; that present in greater amount was *NN'*-di-2-imidazolinylethylenediamine dipicrate, m. p. 253—255°, as proved by its identity with the product from ethylenediamine and 2-methylthioimidazoline [3] or on 2-nitroiminoimidazolidine.[7]



(II) (III)

The second picrate, m. p. 204°, was the dipicrate of *N*-2-imidazolinylethylenediamine, obtained by the action of an excess of ethylenediamine on 2-nitroiminoimidazolidine. 2,3,5,6-Tetrahydro-1*H*-imidaz[1,2*a*]imidazole (III) has been obtained as the monopicrate, m. p. 219—221°, by McKay and his co-workers [8] by a variety of methods; we have confirmed this melting point.

In view of their pharmacological interest a number of 2-aryl(or alkyl)amino-2-oxazolines, some of which show vascular activity,[9] have been prepared by analogous procedures from amino-alcohols. The preparation of guanidinoethanol itself from ethanolamine hydrobromide and cyanamide has been described.[10] 2-Amino-2-oxazolines have also been synthesised by cyclisation of *N*-aryl-*N'*-2-halogenoethylureas [11] in boiling water and by simultaneous dethionation and ring closure of *N*-aryl-*N'*-2-hydroxyethylthioureas (VI) by mercuric oxide in an inert solvent.[12] In the present work some carbodi-imides were caused to react with amino-alcohols.



(IV) (V) (Va) (VI) (VII)

Diphenylcarbodi-imide thus gives exothermally the *NN'*-diphenylguanidinoethanols (IV; $R^5$ = Ph) in good yield. Heating these in boiling xylene results in elimination of aniline with production of 2-anilino-2-oxazolines (Va; $R^5$ = Ph) also in good yield. Some new oxazolines have been prepared by this method, but the instability of the dialkylcarbodi-imides and the difficulty of isolation of the products when substituted diphenylcarbodi-imides were used prevented extension of the method.

2-Phenyl(or methyl)amino-2-oxazolines (Va; $R^5$ = Me or Ph) are also produced in good yield by the action of methyl iodide followed by sodium ethoxide on *N*-2-hydroxyethyl-*N'*-phenyl(or methyl)thioureas (VI; $R^5$ = Me or Ph) in boiling ethanol. The reaction presumably proceeds through the isothiouronium salt (VII), a route suggested by Goldberg and Kelly [13] who prepared 2-alkyl(and aryl)-2-oxazolines from thioamides by a

[7] McKay, Coleman, and Grant, *J. Amer. Chem. Soc.*, 1950, **72**, 3205.
[8] McKay, Kreling, Paris, Braun, and Whittingham, *Canad. J. Chem.*, 1957, **35**, 843; McKay, Hatton, and Braun, *J. Amer. Chem. Soc.*, 1956, **78**, 6144.
[9] Giudicelli, Beauvallet, Chabrier, and Najer, *Compt. rend.*, 1958, **247**, 891; *ibid.*, p. 2494.
[10] Fromm, Fantle, and Fisch, *J. prakt. Chem.*, 1929, (2), **124**, 167; Schering and Kahlbaum, D.R.P. 462,995; (*a*) Fishbein and Gallaghan, *J. Org. Chem.*, 1956, **21**, 434.
[11] Gabriel and Stelzner, *Ber.*, 1895, **28**, 2929; (*a*) Najer, Chabrier, and Giudicelli, *Bull. Soc. chim. France*, 1959, 532, 1611.
[12] Söderbaum, *Ber.*, 1895, **28**, 1897; Dains, *J. Amer. Chem. Soc.*, 1925, **47**, 1981.
[13] Goldberg and Kelly, *J.*, 1948, 1919.

similar method. In the preparation of 2-anilino-2-oxazoline by this method 1-phenyl-2-imidazolidone was formed as a by-product. Attempts to produce this from phenylurea and ethylenediamine by a published method [14] gave 2-imidazolidone, aniline, and ammonia. A specimen of 1-phenyl-2-imidazolidone was prepared for comparison by the method described by McKay and Braun.[15]

## Experimental

*2-Aminoimidazoline.*—(A) Ethylenediamine dihydrochloride (2·7 g., 1 mol.) and *S*-methylisothiouronium sulphate (2·8 g., 1·5 mol.) were dissolved in water (10 ml.), brought to pH 7 with sodium hydrogen carbonate solution, and heated on the steam bath for 2 hr. The residue left after evaporation of the water crystallised from ethanol to give the somewhat hygroscopic *2-aminoethylguanidinium sulphate*, m. p. 298° (decomp.) (Found: C, 15·4; H, 6·5. $C_3H_{10}N_4,H_2SO_4,2H_2O$ requires C, 15·3; H, 6·8%). The *picrate* had m. p. 246° (Found: C, 32·4; H, 2·7. $C_{15}H_{16}N_{10}O_{14}$ requires C, 32·15; H, 2·9%). The aminoethylguanidinium sulphate (2 g., 1 mol.) was passed in water through Amberlite IRA-400 (OH) resin and evaporated under reduced pressure to a hygroscopic oil from which 2-aminoimidazoline picrate, m. p. 223° (decomp.) (Pierron [1] gave 217°) was obtained as needles from ethanol (Found: C, 34·4; H, 3·3. Calc. for $C_9H_{10}N_6O_7$: C, 34·4; H, 3·2%).

(B) Ethylenediamine monotoluene-*p*-sulphonate (11·6 g., 1 mol.) was heated on the steam bath with cyanamide (4·2 g., 2 mol.) for 3 hr., during which ammonia was given off. The residual syrup was triturated with hot ethanol (30 ml.) and, after cooling, the crystals of *ethylenediguanidinium ditoluene*-p-*sulphonate* (5·5 g.), m. p. 292°, were collected (Found: C, 44·8; H, 6·0. $C_{18}H_{28}N_6O_6S_2$ requires C, 44·3; H, 5·7%). The free *base*, hygroscopic prisms from ethanol–ether, had m. p. 165° (Found: C, 31·3; H, 8·4; N, 55·0. Calc. for $C_4H_{12}N_6,\frac{1}{2}H_2O$: C, 31·4; H, 8·5; N, 54·9%); (lit.,[16] m. p. 163°). The *hydrochloride*, prismatic needles from ethanol–ether, had m. p. 228° (Found: C, 22·5; H, 6·6. $C_4H_{12}N_6,2HCl$ requires C, 22·1; H, 6·5%). The mother liquors from the above toluenesulphonate gave, on evaporation, *2-aminoimidazoline toluene*-p-*sulphonate*, prismatic needles (from ethanol) (2·6 g., 20%), m. p. 195° (Found: C, 46·6; H, 6·1. $C_{10}H_{15}N_3O_3S$ requires C, 46·7; H, 5·8%). The free base, a syrup, was obtained by treatment of the toluene-*p*-sulphonate with Amberlite IRA-400 and converted into the hygroscopic hydrochloride, needles (from ethanol–ethyl acetate), m. p. 140° (Pierron [1] reports 120—122°) (Found: C, 29·6; H, 6·9; N, 35·0. Calc. for $C_3H_7N_3,HCl$: C, 29·6; H, 6·6; N, 34·5%). The picrate, needles from aqueous ethanol, had m. p. 223° (decomp.) (Pierron [1] gives 217°) (Found: C, 34·4; H, 3·3. Calc. for $C_9H_{10}N_6O_7$: C, 34·4; H, 3·2%). The sulphate, hydrobromide, and nitrate had m. p.s as reported.

(C) Ethylenediamine monotoluene-*p*-sulphonate (5·8 g., 1 mol.) and dimethylcyanamide (1·8 g., 1 mol.) were heated over an open flame for a few seconds to induce the exothermic reaction, which took place with the evolution of dimethylamine. After further heating on the steam bath for 3 hr., the semicrystalline mass was dissolved in hot ethanol and allowed to crystallise (yield: 3·0 g., 46%; m. p. 195°).

*2-Amino-1,4,5,6-tetrahydropyrimidine.*—(A) Trimethylenediamine ditoluene-*p*-sulphonate (10·45 g., 1 mol.), the free diamine (1·85 g., 1 mol.), and dimethylcyanamide (3·5 g., 2 mol.) were heated over a free flame until an exothermic reaction took place, and then on the water bath for 10 min. Crystallisation from ethanol gave *2-amino-1,4,5,6-tetrahydropyrimidine monotoluene*-p-*sulphonate* (7 g., 52%), m. p. 175° (Found: C, 48·5; H, 6·2. $C_{11}H_{17}N_3O_3S$ requires C, 48·7; H, 6·3). The picrate (from ethanol) had m. p. 184° (Found: C, 36·5; H, 3·8. Calc. for $C_{10}H_{12}N_6O_7$: C, 36·6; H, 3·6%) (lit.,[10a] m. p. 188—200°).

(B) Trimethylenediamine ditoluene-*p*-sulphonate (3 g., 1 mol.), the free diamine (0·53 g., 1 mol.), and cyanamide (0·9 g., 1·5 mol.) were heated on the water bath for 45 min. The solid residue crystallised from ethanol to give 2-amino-1,4,5,6-tetrahydropyrimidine monotoluene-*p*-sulphonate, m. p. 175° (2·3 g., 59%). The mother liquors contained trimethylenediguanidine which was precipitated as the dipicrate,[18] m. p. 242° (1 g., 1·1%) (Found: C, 32·9; H, 3·15. Calc. for $C_{17}H_{20}N_{12}O_{14}$: C, 33·2; H, 3·2%).

[14] U.S.P. 2,517,750.
[15] McKay and Braun, *J. Org. Chem.*, 1951, **16**, 1829.
[16] Jap. P. 154,050.
[17] Stefanye and Howard, *J. Amer. Chem. Soc.*, 1955, **77**, 761.
[18] Schenck and Kirchhof, *Z. physiol. Chem.*, 1926, **158**, 107.

XUM

**2-*Amino*-4-*methylimidazoline*.**—(*A*) Propylenediamine monotoluene-*p*-sulphonate (12·3 g., (1 mol.) was heated gently over a free flame with dimethylcyanamide (3·5 g., 1 mol.) until an exothermic reaction took place, and then for a further 2·5 hr. on the water bath. Crystallisation from ethanol–ether gave 2-*amino*-4-*methylimidazoline monotoluene*-p-*sulphonate* (6·2 g., 46%) as needles, m. p. 135° (Found: C, 48·8; H, 6·5. $C_{11}H_{17}N_3O_3S$ requires C, 48·7; H, 6·3%). The *nitrate*, colourless leaflets from ethanol–ether, had m. p. 87° (Found: C, 29·6; H, 6·0. $C_4H_{10}N_4O_3$ requires C, 29·6; H, 6·2%), and the *picrate*, needles from aqueous ethanol, had m. p. 195° (Found: C, 37·0; H, 3·9. $C_{10}H_{12}N_6O_7$ requires C, 36·6; H, 3·7%).

(*B*) Propylenediamine monotoluene-*p*-sulphonate (1 mol.) and cyanamide (1 mol.) were heated on the water bath for 3 hr. Crystallisation from ethanol gave a small yield of 2-amino-4-methylimidazoline monotoluene-*p*-sulphonate.

**2-*Anilino*-4-*methylimidazoline*.**—Propylenediamine monotoluene-*p*-sulphonate (6·15 g., 1 mol.) and phenylcyanamide (5·9 g., 2 mol.) were heated together on the water bath for 3 hr. The oily residue was converted into 2-*anilino*-4-*methylimidazoline picrate*, m. p. 148° (Found: C, 47·8; H, 4·1. $C_{16}H_{16}N_6O_7$ requires C, 47·5; H, 4·0%). The picrate in aqueous ethanol was passed through a column of IRA-400 ($OH^-$) resin. Evaporation of the eluate under reduced pressure gave 2-anilino-4-methylimidazoline, colourless needles (from benzene), m. p. 81° (Found: C, 68·4; H, 7·5. $C_{10}H_{13}N_3$ requires C, 68·6; H, 7·4%).

**2-*Anilino*-1,4,5,6-*tetrahydropyrimidine*.**—Trimethylenediamine ditoluene-*p*-sulphonate (10·45 g., 1 mcl.), the free diamine (1·85 g., 1 mol.), and phenylcyanamide (5·9 g., 2 mol.) were heated over a free flame until an exothermic reaction set in and then for 2 hr. on the water bath. The residue was crystallised from ethanol to give 2-*anilino*-1,4,5,6-*tetrahydropyrimidine monotoluene*-p-*sulphonate* as prismatic needles, m. p. 167° (5 g., 29%) (Found: C, 58·8; H, 5·8. $C_{17}H_{21}N_3O_3S$ requires C, 58·9; H, 6·1%). The *picrate* (from aqueous ethanol) had m. p. 200° (Found: C, 47·8; H, 4·0. $C_{16}H_{16}N_6O_7$ requires C, 47·5; H, 4·0%).

**2-*Amino*-3a,4,5,6,7,7a-*hexahydrobenzimidazole*.**—*Cyclohexane*-1,2-*diamine monotoluene*-p-*sulphonate* (7·2 g., 1 mol.), prepared by crystallising equimolecular amounts of the diamine and the acid from ethanol (m. p. 181°) (Found: C, 54·2; H, 7·5. $C_{13}H_{22}O_3N_2S$ requires C, 54·5; H, 7·7%), and dimethylcyanamide (3·5 g., 2 mol.) were heated together over the open flame to start the reaction, then further heated for 3 hr. on the steam bath. The product, crystallised from ethanol–ether, gave the 2-*aminohexahydrobenzimidazole toluene*-p-*sulphonate* (1·2 g.), m. p. 233° (Found: C, 54·2; H, 7·0. $C_{14}H_{21}N_3O_3S$ requires C, 54·0; H, 6·8%). The *picrate*, needles from aqueous ethanol, had m. p. 188° (Found: C, 42·1; H, 4·7. $C_{13}H_{16}N_6O_7$ requires C, 42·4; H, 4·4%). The *nitrate*, prisms from ethanol, had m. p. 201° (Found: C, 41·4; H, 7·0. $C_7H_{13}N_3,HNO_3$ requires C, 41·6; H, 6·9%). The free *base*, needles from ethanol, had m. p. 174° (Found: C, 60·2; H, 9·2. $C_7H_{13}N_3$ requires C, 60·4; H, 9·4%).

**2-*Aminobenzimidazole*.**—*o*-Phenylenediamine monotoluene-*p*-sulphonate (9·2 g., 1 mol.) was heated with cyanamide (1·4 g., 1 mol.) at 180° for 8 hr., evolution of ammonia then having ceased. Crystallisation from ethanol gave 2-*aminobenzimidazole toluene*-p-*sulphonate* (4·6 g., 46%), prisms, m. p. 190·5—191·5° (Found: C, 54·9; H, 4·7; N, 14·15; S, 10·8. $C_{14}H_{15}N_3SO_3$ requires C, 55·0; H, 4·9; N, 13·8; S, 10·5%). Crystallisation from benzene–light petroleum (b. p. 60—80°) gave 2-aminobenzimidazole as plates, m. p. and mixed m. p. 222°.

**2-*Dimethylaminobenzimidazole*.**—(*A*) *o*-Phenylenediamine monotoluene-*p*-sulphonate (12 g., 1 mol.) was heated at 160° for 24 hr. with dimethylcyanamide (3 g., 1 mol.); evolution of basic fumes had then ceased. The residue was crystallised repeatedly from ethanol to give 2-*dimethylaminobenzimidazole monotoluene*-p-*sulphonate*, needles, m. p. 256—257° (decomp.) (1·75 g., 12%) (Found: C, 57·45; H, 5·7; N, 12·5. $C_{16}H_{19}N_3SO_3$ requires C, 57·7; H, 5·8; N, 12·6%). The salt was triturated with sodium hydroxide solution and filtered. Crystallisation from ethanol gave 2-dimethylaminobenzimidazole as needles, m. p. 312—313° (Found: C, 67·4; H, 6·7. Calc. for $C_9H_{11}N_3$: C, 67·1; H, 6·8%).

(*B*) 2-Chlorobenzimidazole (1·5 g., 1 mol.) was heated with dimethylamine hydrochloride (0·9 g., 1·1 mol.), potassium hydroxide (1·2 g., 2·1 mol.), and water (8 ml.) at 155—160° for 6 hr. The crystalline product, recrystallised from ethanol, gave 2-dimethylaminobenzimidazole, needles, m. p. 312—314° (1·4 g., 87%).

**2-*Anilinoimidazoline*.**—(*A*) Ethylenediamine monotoluene-*p*-sulphonate (5 g., 1 mol.) and phenylcyanamide (5 g., 2 mol.) were heated on the steam bath for 3 hr., after which ammonia ceased to be evolved. The semi-solid mass of impure toluenesulphonate (1·4 g.) was dissolved in hot alcohol and allowed to crystallise. Treatment of this material with aqueous picric acid

gave *2-anilinoimidazoline picrate*, m. p. 193°, needles from ethanol (Found: C, 46·4; H, 3·9. $C_{15}H_{14}N_6O_7$ requires C, 46·2; H, 3·6%). A solution of the picrate in aqueous ethanol, passed through Amberlite IRA-400, gave on evaporation the free base, m. p. 135° (lit.,[19] m. p. 136°), plates from ethanol (Found: C, 66·8; H, 6·9. Calc. for $C_9H_{11}N_3$: C, 67·1; H, 6·8%); this gave the *hydrochloride*, m. p. 212°, plates from ethanol (Found: C, 55·0; H, 6·3. $C_9H_{11}N_3$,HCl requires C, 54·7; H, 6·1%). From the above impure toluenesulphonate it was possible to obtain by fractional crystallisation a small quantity of *ethylenedi-(N-phenylguanidine)*, m. p. 183°, prismatic needles from ethanol (Found: C, 64·9; H, 6·9. $C_{16}H_{20}N_6$ requires C, 64·9; H, 6·8%) [*dihydrochloride*, m. p. 230°, needles from aqueous ethanol (Found: C, 51·6; H, 6·2; N, 22·6. $C_{16}H_{20}N_6$,2HCl requires C, 52·0; H, 6·0; N, 22·8%)].

(*B*) 2-Methylthioimidazoline hydriodide (2·4 g., 1 mol.) and aniline (2·8 g., 3 mol.) were heated at 130° for 3 hr.; then methanethiol ceased to be evolved. Ethanol was then added and the sparingly soluble crystalline material, which did not give a picrate, was removed. The picrate, m. p. 193°, prepared from the filtrate, was passed in solution through the ion-exchange resin to give the free base, m. p. 135°, identical with the product prepared as above.

(*C*) Ethylenediamine monotoluene-*p*-sulphonate (5 g., 1 mol.) was boiled in ethanol (100 ml.) with diphenylcarbodi-imide (4·175 g., 1 mol.) for 4 hr. The solvent and aniline were removed *in vacuo* and the oily residue crystallised from ethanol–ether, to give *2-anilinoimidazoline monotoluene-*p*-sulphonate* (6·2 g., 86%), needles, m. p. 133—134° (Found: C, 57·6; H, 5·9. $C_{16}H_{19}N_3O_3S$ requires C, 57·7; H, 5·7%). The picrate had m. p. 195°, alone or mixed with the specimen from the previous preparation. The free base was prepared from the toluenesulphonate by treatment with Amberlite IRA-400 ($OH^-$) resin.

*NN′-Di-2-imidazolinylethylenediamine*.—This was produced as the dipicrate by the methods described by McKay *et al.*[7] and Aspinall and Bianco;[3] it had m. p. 254—255° (lit., m. p. 268—269,[7] 259—261°[3]) (Found: C, 36·6; H, 3·5; N, 25·3. Calc. for $C_{20}H_{22}N_{12}O_{14}$: C, 36·75; H, 3·4; N, 25·6%).

N-2-*Imidazolinylethylenediamine*.—The dipicrate, made as described by McKay *et al.*,[7] had m. p. 204° (lit., m. p. 205—206·5°) (Found: C, 35·0; H, 3·4; N, 24·25. Calc. for $C_{17}H_{16}N_{10}O_{14}$: C, 34·9; H, 3·1; N, 23·9%).

2-Amino-2-imidazoline hydrobromide (1·9 g., 1 mol.) in water was mixed with ethylenediamine (0·7 g., 1 mol.) and heated at 100° for 48 hr. Further ethylenediamine (1·4 g., 2 mol.) was added during the first 40 hr. After being heated finally at 130—150° for 2 hr. to remove the excess of ethylenediamine, the residue was converted into the picrate. Crystallisation from ethanol gave a small yield of *N*-2-imidazolinylethylenediamine dipicrate, m. p. 204°. The ethanol-insoluble material crystallised from aqueous ethanol to give *NN′*-di-2-imidazolinylethylenediamine dipicrate, m. p. 253—255°.

N-2-*Hydroxyethyl-N′-phenylthiourea*.—Phenylisothiocyanate (20 g., 1 mol.) was slowly added to a solution of ethanolamine (9·04 g., 1 mol.) in benzene (100 ml.). An exothermic reaction took place and the mixture was left at room temperature for 2 hr. The product crystallised from ethanol as needles, m. p. 139° (Knorr and Rossler[20] report 138°) (28 g., 96·5%).

New *thioureas* prepared in this way were: N-(2-*hydroxy*-1-*phenylethyl*)-N′-*phenyl*- (VI; $R^1 = R^5 = Ph$, $R^2 = R^3 = H$), m. p. 164°, needles from ethanol, in 91% yield (Found: C, 66·2; H, 5·8. $C_{15}H_{16}N_2OS$ requires C, 66·1; H, 5·9%); N-2-*hydroxyethyl*-N′-*methyl*- (VI; R's = H, except $R^5$ = Me), m. p. 73°, prisms from chloroform–light petroleum, in 70% yield (Found: C, 35·7; H, 7·7. $C_4H_{10}N_2OS$ requires C, 35·9; H, 7·45%); *N*-(2-hydroxy-1,1-dimethylethyl)-*N′*-phenyl- (VI; $R^1 = R^2 = Me$, $R^3 = H$, $R^5 = Ph$), m. p. 131° (lit.,[21] 127—128·5°) (Found: C, 59·0; H, 7·4. Calc. for $C_{11}H_{16}N_2OS$; C, 59·0; H, 7·15%).

2-*Imidazolidone*.—Phenylurea (10 g., 1 mol.) was heated with ethylenediamine hydrate (20 g., 3·5 mol.) in toluene (150 ml.) at 100° for 4 hr. The temperature was raised to 140° for 2 hr. and the excess of diamine distilled off together with the solvent and some ammonia. Heating at 150—160°/15 mm. removed aniline, and the residue solidified. Crystallisation from chloroform gave 2-imidazolidone, colourless prisms (4 g., 63%), m. p. 132° (lit.,[22] 131°), and not 1-phenyl-2-imidazolidone as claimed earlier.[14]

[19] G.P. 842,065.
[20] Knorr and Rossler, *Ber.*, 1903, **36**, 1280.
[21] VanderWerf, Heisler, and McEwen, *J. Amer. Chem. Soc.*, 1954, **76**, 1231.
[22] Tafel and Reindl, *Ber.*, 1901, **34**, 3288.



XUM

N-2-*Hydroxyethyl*-N′N″-*diphenylguanidine* (IV; R's = H except $R^5$ = Ph).—Ethanolamine (1 g., 1 mol.) in benzene (10 ml.) was added to diphenylcarbodi-imide (3·2 g., 1 mol.) in benzene (10 ml.). An exothermic reaction took place. After 1 hr. the solvent was removed *in vacuo* and the residue crystallised from chloroform–light petroleum (b. p. 40—60°) to give the *guanidine*, needles, m. p. 109—110° (3·9 g., 93%) (Found: C, 70·4; H, 6·5. $C_{15}H_{17}N_3O$ requires C, 70·6; H, 6·6%).

Also prepared by this method were N-2-*hydroxypropyl*-N′N″-*diphenyl*-, needles, m. p. 157° [from chloroform–light petroleum (b. p. 40—60°); 60% yield] (Found: C, 71·2; H, 7·1; N, 15·45. $C_{16}H_{19}N_3O$ requires C, 71·4; H, 7·1; N, 15·6%), and N′-2-*hydroxyethyl*-N-*methyl*-N″-*diphenyl-guanidine*, needles, m. p. 129—130° [from benzene–light petroleum (b. p. 40—60°); 69% yield] (Found: C, 71·1; H, 7·2; N, 15·7. $C_{16}H_{19}N_3O$ requires C, 71·4; H, 7·1; N, 15·6%).

Other guanidino-compounds prepared were cyclised directly without isolation.

2-*Anilino*-2-*oxazoline*.—(*A*) *N*-2-Hydroxyethyl-*N′N″*-diphenylguanidine (1·95 g.) was refluxed in xylene for 0·5 hr., and the solvent removed together with aniline. Crystallisation from chloroform–light petroleum (b. p. 40—60°) gave 2-anilino-2-oxazoline,[11] colourless needles, m. p. 119—120° (1·14 g., 92%) (Found: C, 66·9; H, 6·2; N, 17·1. Calc. for $C_9H_{10}N_2O$: C, 66·7; H, 6·2; N, 17·3%). The picrate had m. p. 187° (decomp.) (lit.,[11] 175°) (Found: C, 45·8; H, 3·3. Calc. for $C_{15}H_{13}N_5O_8$: C, 46·0; H, 3·3%).

(*B*) *N*-2-Hydroxyethyl-*N′*-phenylthiourea (7 g., 1 mol.) in ethanol (70 ml.) was refluxed with methyl iodide (7·6 g., 1·5 mol.) for 1 hr. Sodium ethoxide [from sodium (2·05 g., 2·5 mol.) in ethanol (80 ml.)] was added and the mixture refluxed (further 3 hr.) until evolution of methanethiol ceased. The solvent was removed *in vacuo* and water (100 ml.) added. After cooling to 5°, the colourless solid was collected and washed with ice-water. Crystallisation as above gave 2-anilino-2-oxazoline (3·9 g., 67%). The alkaline mother liquors were extracted

2-(Substituted amino)-2-oxazolidines (V) and -oxazolines (Va) and their derivatives.

| | | | | | | Yield[g] | | Found (%) | | | | Required (%) | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| $R^1$ | $R^2$ | $R^3$ | $R^4$ | $R^5$ | Method | (%) | M. p. | C | H | N | Formula | C | H | N |
| H | H | H | H | Ph | A | 86[e] | 119—120°[h] | 66·9 | 6·2 | 17·1 | $C_9H_{10}N_2O$ | 66·7 | 6·2 | 17·3 |
| | | | | | B | 67 | | | | | | | | |
| Picrate[b] | | | | | | | 187[i] | 45·8 | 3·3 | — | $C_{15}H_{13}N_5O_8$ | 46·0 | 3·3 | — |
| H | H | H | H | Me | B | 40[e] | 106—108 | 47·7 | 8·2 | 28·4 | $C_4H_8N_2O$ | 48·0 | 8·0 | 28·0 |
| Picrate[e] | | | | | | | 165—166[p] | 36·6 | 3·55 | — | $C_{10}H_{11}N_5O_8$ | 36·5 | 3·35 | — |
| Et | H | H | H | Ph | A | 61[d] | 100—101[j] | 69·3 | 7·6 | 14·6 | $C_{11}H_{14}N_2O$ | 69·5 | 7·4 | 14·7 |
| | | | | | B | 50 | | | | | | | | |
| Picrate[e] | | | | | | | 135 | 48·7 | 4·2 | — | $C_{17}H_{17}N_5O_8$ | 48·7 | 4·1 | — |
| Ph | H | H | H | Ph | A | 69[d] | 156—157 | 75·4 | 5·9 | 11·75 | $C_{15}H_{14}N_2O$ | 75·6 | 5·9 | 11·8 |
| | | | | | B | 80 | | | | | | | | |
| Picrate[b] | | | | | | | 196 | 53·8 | 3·6 | — | $C_{21}H_{17}N_5O_8$ | 54·0 | 3·6 | — |
| H | H | Me | H | Ph | A | 55[e] | 134[km] | 68·2 | 6·7 | 15·8 | $C_{10}H_{12}N_2O$ | 68·2 | 6·8 | 15·9 |
| | | | | | B | 82 | | | | | | | | |
| Picrate | | | | | | | 169[n] | 47·5 | 3·8 | — | $C_{16}H_{15}N_5O_8$ | 47·5 | 3·7 | — |
| Me | Me | H | H | Ph | A | 70 | 114—116 | 69·4 | 7·3 | 14·9 | $C_{11}H_{14}N_2O$ | 69·5 | 7·4 | 14·7 |
| | | | | | B | 85 | | | | | | | | |
| Picrate[b] | | | | | | | 205 | 48·5 | 4·2 | — | $C_{17}H_{17}N_5O_8$ | 48·7 | 4·1 | — |
| H | H | H | Me | Ph | A | 65[d] | 82 | 68·4 | 6·55 | 15·7 | $C_{16}H_{12}N_2O$ | 68·2 | 6·8 | 15·9 |
| Hydrochloride[f] | | | | | | | 111 | 56·5 | 6·05 | — | $C_{10}H_{13}ClN_2O$ | 56·5 | 6·1 | — |
| Me | H | Ph | H | Ph | A | 71[e] | 140 | 76·0 | 6·3 | 11·5 | $C_{16}H_{16}N_2O$ | 76·2 | 6·3 | 11·1 |
| Hydrochloride[f] | | | | | | | 156 | 66·3 | 6·5 | 9·9 | $C_{16}H_{17}ClN_2O$ | 66·4 | 6·7 | 9·7 |
| Me | H | Ph | Me | Ph | A | | | | | | | | | |
| Hydrochloride[g] | | | | | | | 84 | 187 | 67·5 | 6·4 | — | $C_{17}H_{19}ClN_2O$ | 67·3 | 6·3 | — |

Crystallised from (*a*) chloroform–light petroleum (b. p. 40—60°), (*b*) aqueous ethanol, (*c*) water, (*d*) benzene–light petroleum, (*e*) ethanol, (*f*) ether–light petroleum, (*g*) ethanol–ether.

Recorded m. p.: (*h*) [11] 119—120°; (*i*) [11] 175°; (*j*) [11a] 102°; (*k*) [11a] 141°; (*m*) [33] 132°; (*n*) [33] 166—168°; (*p*) [34] 167°.

(*q*) Yields by method A are overall based on the amino-alcohol.

The optically active amino-alcohols were the (±)-forms except that (−)-ephedrine was used for the preparation of 3,4-dimethyl-5-phenyl-2-phenylimino-oxazolidine. β-Aminophenethyl alcohol was prepared from styrene oxide and sodium azide.[35]

[33] Meene, *Ber.*, 1900, **33**, 657.
[34] McKay, *Canad. J. Chem.*, 1953, **31**, 284.
[35] McEwen, Conrad, and VanderWerf, *J. Amer. Chem. Soc.*, 1952, **74**, 1168.

with chloroform (5 × 80 ml.). The colourless residue left on evaporation was washed with dilute hydrochloric acid (20 ml.) and then with water. Crystallisation from chloroform–light petroleum gave 1-phenyl-2-imidazolidone, needles (0·1 g., 1·7%), m. p. 162—163°, not depressed by a specimen prepared by the method of McKay and Braun [15] (Found: C, 66·6; H, 6·0; 17·3. Calc. for $C_9H_{10}N_2O$: C, 66·7; H, 6·2; N, 17·3%).

The Table lists the oxazolidines and oxazolines produced by these methods.

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## 1015. *Iodomercurate Complexes with Group V Quaternary Iodides. Part II.*[1] *Reactions with Triphenylphosphine.*

By G. B. DEACON and B. O. WEST.

Triphenylphosphine reacts with a representative of each of the main stoicheiometric classes of the "quaternary" iodomercurates * in acetone or ethanol, with the formation of an iodo(triphenylphosphine)-mercury(II) complex, and either a "quaternary" iodomercurate with a higher iodine : mercury ratio than the reactant or a "quaternary" iodide.

GALLAIS [2] prepared the compounds $MHgI_3,H_2O$ (where M is K or $NH_4$) and suggested that they were not solvates but contained the tetraco-ordinate ion $[HgI_3,H_2O]^-$. Recently the preparation of the nickel complexes $[NEt_4][Ph_3P,NiX_3]$ (where X is Br or I) has been reported.[3] We have attempted to provide an unequivocal example of a mercury complex of the type $[HgI_3Y]^-$ (where Y is a neutral molecule) by the reaction between equimolar amounts of pyridinium tri-iodomercurate(II) and triphenylphosphine in acetone. The expected complex $[PyH][Ph_3P,HgI_3]$ was not isolated, the products being di-iodobis-(triphenylphosphine)mercury(II) [4] and dipyridinium tetraiodomercurate(II).[1,5] The former product was still obtained when the ratio of iodomercurate to phosphine was 2 : 1.

The reaction of triphenylphosphine (2 mol.) with dipyridinium tetraiodomercurate (1 mol.) also gave di-iodobis(triphenylphosphine)mercury(II) as one product and pyridinium iodide as the other. However, compounds representing the other two classes of iodomercurates, *viz.*, $[PyH]_2Hg_3I_8$ and $[PMe_4][Hg_2I_5]$, gave different phosphine–mercuric iodide complexes depending on the ratio of triphenylphosphine to iodomercurate. With a 2 : 1 ratio of phosphine to iodomercurate the di-iodobis(triphenylphosphine)mercury complex was obtained while with a 1 : 1 ratio the new compound di-iodotriphenylphosphine-mercury(II) was formed. The appropriate tri-iodomercurate was formed as the second product in each reaction.

The reactions may be represented:

$$2[PyH][HgI_3] + 2Ph_3P \longrightarrow (Ph_3P)_2HgI_2 + [PyH]_2[HgI_4] \quad \text{(i)}$$

$$[PyH]_2[HgI_4] + 2Ph_3P \longrightarrow (Ph_3P)_2HgI_2 + PyH{\cdot}I \quad \text{(ii)}$$

$$[PyH]_2[Hg_3I_8] + nPh_3P \longrightarrow (Ph_3P)_nHgI_2 + 2[PyH][HgI_3] \quad \text{(iii)}$$

$$[PMe_4][Hg_2I_5] + nPh_3P \longrightarrow (Ph_3P)_nHgI_2 + [PMe_4][HgI_3] \quad \text{(iv)}$$

where $n = 1$ or 2.

The compound di-iodotriphenylphosphinemercury(II) is assumed to be a dimer by

* $M_2HgI_4$, $MHgI_3$, $MHg_2I_5$, and $M_2Hg_3I_8$, where M is a quaternary cation.

[1] Part I, Deacon and West, *J.*, 1961, 3929.
[2] Gallais, *Ann. Chim.* (*France*), 1938, **10**, 117.
[3] Cotton and Goodgame, *J. Amer. Chem. Soc.*, 1960, **82**, 2967.
[4] Evans, Mann, Peiser, and Purdie, *J.*, 1940, 1209.
[5] Lal Datta, *J. Amer. Chem. Soc.*, 1913, **35**, 949; Francois, *Compt. rend.*, 1905, **140**, 861.

analogy with the compounds $R_3P,HgI_2$ prepared by Evans *et al.*[4] which had molecular weights corresponding to dimers. The triphenylphosphine complex was not sufficiently soluble in suitable solvents for its molecular weight to be measured.

The slightly soluble compounds $(Ph_3P)_2HgI_2$ and $(Ph_3P,HgI_2)_2$ can be directly prepared by mixing triphenylphosphine and mercuric iodide in the correct molar proportions in benzene, the complexes being rapidly precipitated. Since the various iodomercurates are known to dissociate into mercuric iodide and iodine in solution a partial explanation of the triphenylphosphine–iodomercurate reactions can be made by assuming that the reaction product, $(Ph_3P)_2HgI_2$ or $(Ph_3P,HgI_2)_2$, is formed by the direct reaction between triphenylphosphine and free mercuric iodide in solution. Formation constants for the various ions in acetone have not been measured but the values in acetonitrile found by Ellendt and Cruse [6] are assumed to indicate the relative stabilities of the species.

$$HgI_2 + I^- \rightleftharpoons [HgI_3]^- \quad K_3 = 9 \times 10^5$$
$$[HgI_3]^- + I^- \rightleftharpoons [HgI_4]^{2-} \quad K_4 = 40$$
$$[HgI_3]^- + HgI_2 \rightleftharpoons [Hg_2I_5]^- \quad K_5 = 10$$

Ellendt and Cruse did not detect the formation of the $[Hg_3I_8]^{2-}$ species in solution, which indicates its extensive dissociation $[Hg_3I_8]^{2-} \rightleftharpoons HgI_2 + 2[HgI_3]^-$. Spectroscopic evidence was presented in Part I [1] to confirm extensive dissociation for this complex ion in ethanol.

Thus in the reactions between triphenylphosphine and either the tri-iodo- or the tetra-iodo-mercurate complexes, since there would be only a small concentration of "free" mercuric iodide in solutions of either complex, the ratio of mercuric iodide to added triphenylphosphine in each of the experiments performed was considerably smaller than the maximum 1 : 2 figure required to afford $(Ph_3P)_2HgI_2$ and therefore that complex was obtained.

Pentaiodo- and octaiodo-complexes dissociate into mercuric iodide and tri-iodomercurate ions so extensively as to produce virtually one molar equivalent of "free" mercuric iodide for every mole of iodomercurate complex; therefore, in these cases the particular triphenylphosphine–mercuric iodide complex formed will depend on the molar ratio of triphenylphosphine to iodomercurate, *i.e.*, 1 : 1 ratios give $(Ph_3PHgI_2)_2$, 2 : 1 give $(Ph_3P)_2HgI_2$.

This hypothesis alone does not account for the low yields of triphenylphosphine–mercuric iodide complexes in all the reactions—the yields are generally lower than those calculated on the basis of equations (i—iv). This may indicate that $[HgI_3,PPh_3]^-$ ions or other, more complex species exist in solution in equilibrium with the precipitated complexes. The reaction between triphenylphosphine and pyridinium tetraiodomercurate requires further investigation in this respect because the product finally obtained, *viz.*, $(Ph_3P)_2HgI_2$, is not immediately precipitated when the reactants are mixed despite its known low solubility in acetone but is only produced on boiling. This behaviour is not shown by any of the other iodomercurates, with which immediate precipitation of the final phosphine–mercuric iodide complex occurs on mixing. The solution of the tetra-iodomercurate will contain a much lower concentration of "free" mercuric iodide than that of any of the other compounds because the iodide ions released in the first stage of dissociation, $[HgI_4]^{2-} \rightleftharpoons [HgI_3]^- + I^-$, restrict further dissociation of the $[HgI_3]^-$ ion. Thus, in this case, triphenylphosphine reacts at room temperature with mainly $[HgI_3]^-$ ions and this system should provide the best opportunity for formation of $[HgI_3PPh_3]^-$ ions if indeed they can exist at all.

When triphenylphosphine in excess was treated with each of the compounds, triphenylmethylphosphonium tri-iodomercurate, dipyridinium octaiodotrimercurate, and tetramethylphosphonium pentaiododimercurate in boiling ethanol, the mercuric iodide in the

[6] Ellendt and Cruse, *Z. phys. Chem.* (*Leipzig*), 1952, **201**, 130.

compounds was quantitatively precipitated as di-iodobis(triphenylphosphine)mercury(II). The reaction may thus be used as an analytical method for the determination of the mercuric iodide content of members of the $MHgI_3$, $MHg_2I_5$, and $M_2Hg_3I_8$ classes of Group VB quaternary iodomercurates. Since the tetraiodomercurate complex is an intermediate in the total decomposition of the tri-iodomercurate complex (reaction i), the method should be satisfactory also for tetraiodomercurate complexes. The liberated quaternary iodide was recovered in each case. Iodomercurates are useful derivatives for the isolation of Group VB quaternary cations from reaction mixtures, and decomposition with triphenylphosphine provides a satisfactory method for the recovery of the quaternary iodide.

## Experimental

*Reaction of Quaternary Iodomercurates with Triphenylphosphine.*—The preparation of the quaternary iodomercurates has been reported.[1] After reactions 1, 5, 7, 8 (below) the products were shown to be identical with authentic samples of the appropriate compounds by comparison of *X*-ray powder photographs.

In reactions 1—6, solutions of the required amounts of triphenylphosphine and the quaternary iodomercurate, each in *ca.* 10 ml. of acetone, were mixed. Rapid precipitation of an iodo(triphenylphosphine)mercury(II) complex occurred. The mixture was left for an hour, then the precipitate was filtered off (fraction A). The filtrate was evaporated and the residue leached with a small quantity of cold acetone. This dissolved the iodomercurate, leaving undissolved some additional iodo(triphenylphosphine)mercury(II) complex (fraction B). Complete removal of the latter complex from the iodomercurate proved difficult, presumably since triphenylphosphine was reacting further in the extract. A further evaporation and extraction, followed by two or more recrystallizations of the iodomercurate from ethanol [ethanol–ether in the case of pyridinium tri-iodomercurate(II)], were generally necessary to achieve satisfactory purity. The two crops of the iodo(triphenylphosphine)–mercury(II) complex were either mixed and recrystallized from boiling benzene or were recrystallized and characterized separately. The stated yields of this complex refer to fraction (A).

Di-iodobis(triphenylphosphine)mercury(II) was synthesized by reaction between stoicheiometric quantities of mercuric iodide and triphenylphosphine in benzene (lit.,[4] ethanol used) and, recrystallized from benzene, had m. p. 246—247° (lit.,[4] *ca.* 250°) (Found: C, 44·0; H, 3·3; I, 26·4. Calc. for $C_{36}H_{30}HgI_2P_2$: C, 44·1; H, 3·1; I, 26·0%).

*Di-iodo(triphenylphosphine)mercury*(II) was synthesized by the reaction between stoicheiometric amounts of mercuric iodide and triphenylphosphine in benzene and, recrystallized from benzene, had m. p. 242—242·5° (Found: C, 30·6; H, 2·2; I, 35·4. $C_{18}H_{15}HgI_2P$ requires C, 30·2; H, 2·1; I, 35·4%). Di-iodo(triphenylphosphine)mercury(II), m. p. 242° (Found: C, 30·0; H, 2·3; I, 35·3%), was also obtained when triphenylphosphine and mercuric iodide reacted in benzene in the stoicheiometric ratio required for the formation of the complex, $(Ph_3P)_2(HgI_2)_3$. It was almost insoluble in cold acetone and benzene, insoluble in cold ethanol, and sparingly soluble in boiling benzene and acetone. Decomposition occurred during a Rast molecular-weight determination, and the solubility of the complex in boiling chloroform was not sufficient to afford a meaningful value of the molecular weight.

*Reactions.*—(1) Pyridinium tri-iodomercurate(II) (1·32 g., 2·0 mmoles) with triphenylphosphine (0·52 g., 2·0 mmoles) yielded di-iodobis(triphenylphosphine)mercury(II) (0·55 g., 0·56 mmole, 56%). The mixture of fractions (A) and (B) had m. p. 250° (Found: C, 44·1; H, 3·0; I, 26·0%). The other product was dipyridinium tetraiodomercurate(II), m. p. 168° (lit.,[1] *ca.* 168°), mixed m. p. 166·5—167°.

(2) Pyridinium tri-iodomercurate(II) (0·66 g., 1·0 mmole) with triphenylphosphine (0·13 g., 0·50 mmole) yielded di-iodobis(triphenylphosphine)mercury(II) (0·10 g., 0·10 mmole, 40%), m. p. and mixed m. p. 245° (Found: C, 44·6; H, 3·2%). The reaction mixture was not further investigated.

(3) Dipyridinium octaiodotrimercurate(II) (0·44 g., 0·25 mmole) with triphenylphosphine (0·13 g., 0·50 mmole) yielded di-iodobis(triphenylphosphine)mercury(II) {0·20 g., 0·20 mmole, 80% based on the reaction $[PyH]_2[Hg_3I_8] + 2Ph_3P \longrightarrow (Ph_3P)_2HgI_2 + 2[PyH][HgI_3]$}, m. p. and mixed m. p. 247—248° (Found: C, 44·4; H, 3·2%). The product obtained as fraction B was not investigated. The other product was pyridinium tri-iodomercurate(II), m. p. and

mixed m. p. 149—150° (lit.,[1] 149·5°) (Found: C, 9·2; H, 1·0; Hg, 29·9. Calc. for $C_5H_6HgI_3N$: C, 9·1; H, 0·9; Hg, 30·3%).

(4) Dipyridinium octaiodotrimercurate(II) (0·89 g., 0·50 mmole) with triphenylphosphine (0·13 g., 0·50 mmole) yielded di-iodo(triphenylphosphine)mercury(II) {0·19 g., 0·27 mmole, 54% based on the reaction $[PyH]_2[Hg_3I_8] + Ph_3P \longrightarrow (Ph_3P,HgI_2) + 2[PyH][HgI_3]$}, m. p. and mixed m. p. 242—242·5° (Found: C, 30·2; H, 2·1%). The product obtained as fraction (B) had m. p. and mixed m. p. 240—240·5° (Found: C, 29·9; H, 2·3%). The other product was pyridinium tri-iodomercurate(II), m. p. and mixed m. p. 149—150° (Found: C, 9·6; H, 1·1; Hg, 29·9%).

The reaction was repeated with double the concentration of each reactant to find whether any di-iodobis(triphenylphosphine)mercury(II) was present in the initially precipitated product. Di-iodo(triphenylphosphine)mercury(II) obtained as fraction (A) was twice recrystallized from benzene, then having m. p. and mixed m. p. 241—241·5° (Found: C, 30·2; H, 2·15%). The mother liquors from each recrystallization were combined, and crystallization from this solution gave white crystals (*ca.* 30 mg.), m. p. 238° (Found: C, 37·1; H, 2·8%), that may be a mixture of the two iodo(triphenylphosphine)mercury(II) complexes.

(5) Tetramethylphosphonium pentaiododimercurate(II) (1·13 g., 1·0 mmole) with triphenylphosphine (0·52 g., 2·0 mmoles) yielded di-iodobis(triphenylphosphine)mercury(II) {0·80 g., 0·82 mmole, 82% based on the reaction $[PMe_4][Hg_2I_5] + 2Ph_3P \longrightarrow (Ph_3P)_2HgI_2 + [PMe_4][HgI_3]$}. The combined products (A) and (B) had m. p. and mixed m. p. 248—249°. The other product was tetramethylphosphonium tri-iodomercurate(II), m. p. and mixed m. p. 196°.

(6) Tetramethylphosphonium pentaiododimercurate(II) (1·13 g., 1·0 mmole) with triphenylphosphine (0·26 g., 1·0 mmole) yielded di-iodo(triphenylphosphine)mercury(II) {0·36 g., 0·50 mmole, 50% based on the reaction $[PMe_4][Hg_2I_5] + Ph_3P \longrightarrow (Ph_3P,HgI_2) + [PMe_4][HgI_3]$}, m. p. 241—241·5°, mixed m. p. 240—241° (Found: C, 30·1; H, 2·3%). The same product obtained as fraction (B) had m. p. 239—241° (Found: C, 30·1; H, 2·2%). The other product was tetramethylphosphonium tri-iodomercurate(II), m. p. and mixed m. p. 196·5—197° [Found: $HgI_2$, 66·9 (by decomposition with excess of triphenylphosphine as described below). Calc. for $C_4H_{12}HgI_3P$: $HgI_2$, 67·6%].

(7) When acetone solutions of dipyridinium tetraiodomercurate(II) (0·44 g., 0·51 mmole) and triphenylphosphine (0·26 g., 1·0 mmole) were mixed no precipitate was obtained. The solution was evaporated to dryness, white crystals being deposited as the volume decreased. After the residue had been extracted with warm ethanol, di-iodobis(triphenylphosphine)-mercury(II) (0·34 g., 0·35 mmole, 70%) remained; recrystallized three times from benzene, it had m. p. and mixed m. p. 248—249°. No crystals were obtained from the ethanol, but it was shown to contain a pyridinium salt by evolution of pyridine on addition of warm aqueous sodium hydroxide.

(8) Dipyridinium tetraiodomercurate(II) (0·44 g., 0·51 mmole) was partially dissolved in ethanol (10 ml.), and a solution of triphenylphosphine (0·26 g., 1·00 mmole) in ethanol (10 ml.) was added. A slight cloudiness developed in the supernatant liquid. The mixture was heated at *ca.* 60°, white crystals being deposited, until the yellow colour of the iodomercurate disappeared from the suspension. The precipitated crystals consisted of di-iodobis(triphenylphosphine)mercury(II) (0·38 g., 0·39 mmole, 78%); twice recrystallized from benzene, this had m. p. and mixed m. p. 249—249·5°. Evaporation of the ethanol yielded an oil which, on addition of ether, gave crystals of impure pyridinium iodide that recrystallized with difficulty from acetone [m. p. 171—173° (decomp.)] (Found: I, 61·1. Calc. for $C_5H_6IN$: I, 61·4%). The ether used to crystallize the pyridinium iodide yielded a small amount of unchanged triphenylphosphine on evaporation.

*Decomposition of Quaternary Iodomercurates by Excess of Triphenylphosphine.—Triphenylmethylphosphonium tri-iodomercurate*(II) was prepared by reaction between stoicheiometric amounts of bis(triphenylmethylphosphonium) tetraiodomercurate(II) [7] and mercuric iodide and, recrystallized from acetone–ethanol, had m. p. 146—146·5° (Found: C, 26·2; H, 2·1; Hg, 22·9. $C_{19}H_{18}HgI_3P$ requires C, 26·5; H, 2·1; Hg, 23·4%).

In reactions (*a*—*c*), boiling ethanol solutions of the iodomercurate and triphenylphosphine [in excess of that required to precipitate all the mercuric iodide of the iodomercurate as $(Ph_3P)_2HgI_2$] were mixed, and di-iodobis(triphenylphosphine)mercury(II) was precipitated. The suspension was maintained at the b. p. of the solvent until the yellow colour disappeared.

[7] Deacon and West, *J. Inorg. Nuclear Chem.*, in the press.

After cooling, the precipitate was filtered off, washed several times with ethanol, dried, and weighed. The filtrate was evaporated to dryness, and ether was added to crystallize the liberated quaternary iodide and dissolve the excess of triphenylphosphine. The quaternary iodide was recrystallized from ethanol–ether or acetone–ether.

(*a*) Triphenylmethylphosphonium tri-iodomercurate(II) (0·256 g., 0·298 mmole) with triphenylphosphine (0·509 g., 1·93 mmoles) yielded di-iodobis(triphenylphosphine)mercury(II) (0·291 g., 0·297 mmole; 100% yield requires 0·292 g.), m. p. (not recrystallized) and mixed m. p. 249—250° (Found: C, 44·6; H, 3·6%). The other product was triphenylmethylphosphonium iodide, m. p. 183—183·5° (lit.,[8,9] 182—183°, 176—181°) (Found: C, 56·5; H, 4·6; I, 30·8. Calc. for $C_{19}H_{18}IP$: C, 56·4; H, 4·5; I, 31·4%).

(*b*) Dipyridinium octaiodotrimercurate(II) (0·482 g., 0·271 mmole) with triphenylphosphine (1·03 g., 3·94 mmoles) yielded di-iodobis(triphenylphosphinemercury(II) (0·792 g., 0·809 mmole; 100% reaction requires 0·796 g.), m. p. (not recrystallized) and mixed m. p. 245—246° (Found: C, 44·1; H, 3·0%). The other product was slightly impure pyridinium iodide, m. p. 171—173° (decomp.) (Found: C, 29·5; H, 3·1; I, 60·2. Calc. for $C_5H_6IN$: C, 29·0; H, 2·9; I, 61·35%).

(*c*) Tetramethylphosphonium pentaiododimercurate(II) (0·455 g., 0·404 mmole) with triphenylphosphine (1·04 g., 3·97 mmoles) yielded di-iodobis(triphenylphosphine)mercury(II) (0·788 g., 0·805 mmole; 100% reaction requires 0·790 g.), m. p. (unrecrystallized) and mixed m. p. 248—249·5° (Found: C, 44·2; H, 3·1%). The other product was tetramethylphosphonium iodide, m. p. >300° (Found: C, 22·5; H, 5·4; I, 57·7. Calc. for $C_4H_{12}IP$: C, 22·0; H, 5·5; I, 58·3%).

Microanalyses were by the C.S.I.R.O. Microanalytical Laboratories, Melbourne. We are grateful to the Department of Geology, University of Adelaide, for the *X*-ray powder photographs, and to the Australian Atomic Energy Commission for the award of a studentship to one of us (G. B. D.).

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The University of Adelaide, South Australia. [*Received, March 17th,* 1961.]

[8] Michaelis and Gleichmann, *Chem. Ber.*, 1882, **15**, 801.
[9] Blount, *J.*, 1932, 337.

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## 1016. *Pteridine Studies. Part XV.*[1] *The Reduction of 2-Hydroxypteridine.*

By Adrien Albert and Sadao Matsuura.

The first example of a reduction in the pyrimidine ring of a pteridine is reported, *viz.*, 2-hydroxypteridine, which gives 3,4-dihydro-2-hydroxypteridine with a variety of reducing agents.

In a new type of 7,8-dihydropteridine synthesis, aminoacetal was condensed with 2,4-dichloro-5-nitropyrimidine to give (eventually) 7,8-dihydro-2-hydroxypteridine. This was reduced to 5,6,7,8-tetrahydro-2-hydroxypteridine.

5,6,7,8-Tetrahydropteridine is the sole product of the reduction [2] of pteridine (I) and hitherto it has been assumed that substituted pteridines, also, are reduced first in the pyrazine ring.[3] However, the principal product of the reduction of 2-hydroxypteridine is the 3,4-dihydro-derivative.

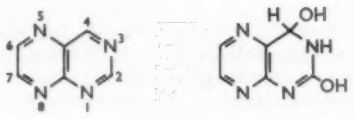
2-Hydroxypteridine resisted reduction in neutral or acidic solution over Raney nickel and Adams platinum catalysts, respectively. However, it was readily reduced to a

[1] Part XIV, Brown and Jacobsen, *J.*, 1961, 4413.
[2] Taylor and Sherman, *J. Amer. Chem. Soc.*, 1959, **81**, 2464.
[3] O'Dell, Vandenbelt, Bloom, and Pfiffner, *J. Amer. Chem. Soc.*, 1947, **69**, 250; Pohland, Flynn, Jones, and Shive, *ibid.*, 1951, **73**, 3247; Cosulich, Roth, Smith, Hultquist, and Parker, *ibid.*, 1952, **74**, 3252.

XUM

dihydro-2-hydroxypteridine in alkaline solution with potassium borohydride, sodium dithionite, or hydrogen (over palladium or nickel). That the anion should be the easily reduced species suggests that reduction takes place at the 3,4-double bond, because this position is masked by covalent hydration to give compound (II) as the stable neutral molecule.[4] However, the anion of 2-hydroxypteridine has a free 3,4-double-bond.[5]

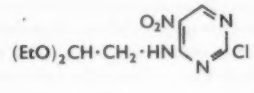
Marked differences exist between the ionization constants and spectra of the reduction product and 7,8-dihydro-2-hydroxypteridine, and different $R_F$ values were found on paper chromatography.



(I)



(II)



(III)

The constitution of the reduction product was established by reduction of 2-hydroxypteridine in deuterium oxide with a hydrogen-free reagent (sodium dithionite). The product was equilibrated with light water by recrystallization and then found to contain only one deuterium atom per molecule (by combustion and infrared measurement of the $D_2O : H_2O$ ratio). This single, unexchangeable deuterium atom in the reduced product must be located on a carbon atom;[6] thus 6,7- and 5,8-hydrogenation, which require 2 and 0 unexchangeable deuterium atoms respectively, were excluded. The constitution was finally shown to be 3,4-dihydro-2-hydroxypteridine by stepwise oxidation of the monodeuterated product to (*a*) 2-hydroxypteridine (with retention of half of the deuterium) and to 2,4-dihydroxypteridine (with complete loss of deuterium). There is, of course, no real distinction between 3,4-dihydro- and 1,4-dihydro-2-hydroxypteridine because the "hydroxy-group" in such substances is largely in the amide form where the hydrogen is sited on a nitrogen atom in the pyrimidine ring.[4,7]

2-Hydroxy-6-methylpteridine, upon reduction, gave a dihydro-derivative so similar in physical properties to that obtained by reducing 2-hydroxypteridine (see Table) that it is assigned the structure 3,4-dihydro-2-hydroxy-6-methylpteridine.

Although there is no recorded method for producing 7,8-dihydropteridines lacking a substituent in the 6-position, 7,8-dihydro-2-hydroxypteridine was obtained by condensing aminoacetal with 2,4-dichloro-5-nitropyrimidine to give 2-chloro-4-(2,2-diethoxyethylamino)-5-nitropyrimidine (III) which was then hydrolysed to the 2-hydroxy-analogue. Reduction of the nitro-group in the latter did not give a useful intermediate unless the acetal group was first hydrolysed by acid. 5-Amino-2-hydroxy-4-methylformamidopyrimidine, formed in this way, cyclized spontaneously to 7,8-dihydro-2-hydroxypteridine in good yield.

7,8-Dihydro-2-hydroxy-6-methylpteridine was obtained by Boon and Jones's method[8] in which aminoacetone (improved preparation given in the Experimental section) was condensed with 2,4-dichloro-5-nitropyrimidine to give 4-acetonylamino-2-hydroxy-5-nitropyrimidine which gave the desired substance on reduction. Oxidation of the product with potassium permanganate furnished 2-hydroxy-6-methylpteridine (mentioned above).

Reduction of 7,8-dihydro-2-hydroxypteridine gave 5,6,7,8-tetrahydro-2-hydroxypteridine whose constitution follows from the resemblance of the ultraviolet spectra to those of 4,5-diamino-2-hydroxypteridine. The resemblance is striking when the three ionic species are compared (Fig. 1), and the displacement of the pteridine spectra to slightly

[4] Brown and Mason, *J.*, 1956, 3443.
[5] Perrin and Inoue, *Proc. Chem. Soc.*, 1960, 342.
[6] Linderstrøm-Lang, Symposium on Peptide Chemistry, *Chem. Soc. Special Publ. No.* 2, 1955, 1.
[7] Albert and Phillips, *J.*, 1956, 1294.
[8] Boon and Jones, *J.*, 1951, 591.

TABLE. Physical properties of pteridines.

| Pteridine | Species (charge) | Ionization in water at 20° p$K_a$ | Spread (±) | Concn.[c] (M) | Spectroscopy in water $\lambda_{max.}$ (mμ) | log ε | pH |
|---|---|---|---|---|---|---|---|
| 2-Hydroxy-[a] | 0 | — | — | — | 230, 307 | 3·88, 3·83 | 7 |
| 2-Hydroxy-6-methyl- | 0 | — | — | — | 235, 315 | 4·05, 3·93 | 7 |
| | − | 11·0 | 0·02 | 0·02 | 261, 377 | 3·87, 3·77 | 13 |
| | + | −0·2 | — | $10^{-4}$ | 240, 310 | 3·96, 3·84 | −2 |
| 3,4-Dihydro-2-hydroxy- | 0 | — | — | — | 248, 317 | 3·72, 3·89 | 7 |
| | − | 12·6 | [b] | $10^{-4}$ | 281, 343 | 3·98, 3·84 | 14 |
| | + | 0 | — | $10^{-4}$ | 254, 337 | 3·78, 3·85 | −2 |
| 3,4-Dihydro-2-hydroxy-6-methyl- | 0 | — | — | — | 248, 321 | 3·83, 3·92 | 7 |
| | − | 13·05 | 0·04 | $10^{-4}$ | 281, 352 | 4·01, 3·84 | 14·2 |
| | + | 0·20 | 0·06 | $10^{-4}$ | 257, 347 | 3·86, 3·88 | −2 |
| 7,8-Dihydro-2-hydroxy- | 0 | — | — | — | 223, 290 | 4·35, 3·88 | 7 |
| | − | [b] | — | — | 308 | 3·95 | 14 |
| | + | 3·50 | 0·02 | 0·02 | 225, *282*, 290, *310* | 3·68, *3·75*, 3·79, *3·75* | 1 |
| 7,8-Dihydro-2-hydroxy-6-methyl | 0 | — | — | — | 220, 287 | 4·46, 3·99 | 7 |
| | − | 11·85 | 0·02 | $10^{-4}$ | 309 | 4·08 | 14 |
| | + | 3·42 | 0·06 | 0·02 | <225, 279, *287*, *310* | >3·7, 4·06, *4·04*, *3·82* | 2 |
| 7,8-Dihydro-2-hydroxy-4,6-dimethyl- | 0 | — | — | — | 222, 289 | 4·39, 4·04 | 7 |
| | − | 12·50 | 0·04 | $10^{-4}$ | 223, 304 | 4·37, 4·10 | 14 |
| | + | 3·99 | 0·02 | 0·01 | <225, 283+ 288, *312* | >3·7, 4·07+ 4·07, *3·90* | 2 |
| 5,6,7,8-Tetrahydro-2-hydroxy- | 0 | — | — | — | 232, 306 | 4·09, 3·70 | 7 |
| | − | 12·5 | — | — | 315 | 3·79 | 14 |
| | + | 4·35 | 0·05 | 0·02 | 229, 327 | 4·00, 3·69 | 1 |

[a] Albert, Brown, and Cheeseman, *J.*, 1951, 474. [b] Instability to alkali prevented determination. [c] The concn. 0·01—0·02M refers to potentiometric, and the $10^{-4}$M, to spectrometric, determinations. [d] In 1 and 4 cm. cells; shoulders in italics.

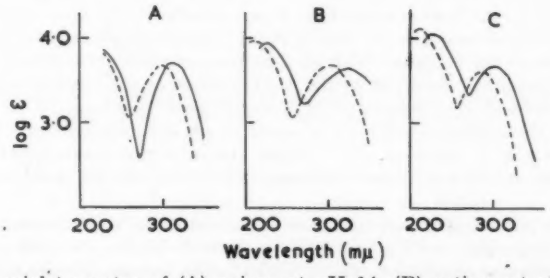



FIG. 1. Ultraviolet spectra of (A) anions at pH 14, (B) cations at pH 1, and (C) neutral molecules at pH 7, of (——) 5,6,7,8-tetrahydro-2-hydroxypteridine, and of (– – – –) 4,5-diamino-2-hydroxypyrimidine.

longer wavelengths is typical.[2] This tetrahydropteridine was identical in $R_F$ and ultraviolet spectra with material isolated chromatographically, in trace amounts insufficient for analysis, from the reduction of 2-hydroxypteridine with potassium borohydride and with hydrogen and nickel.

In unsuccessful attempts to synthesize 2-hydroxy-3,4-dihydropteridine, methyl 3-aminopyrazine-2-carboxylate was reduced to 2-amino-3-hydroxymethylpyrazine. Several attempts to reduce 2-amino-3-cyanopyrazine and 2-amino-3-formylpyrazine oxime to 2-amino-3-aminomethylpyrazine gave only resins. In an attempt to produce 5,6-dihydro-2-hydroxypteridine, glyoxal monoacetal was condensed with 4,5-diamino-2-hydroxypyrimidine to give (after reduction) 4-amino-5-(2,2-diethoxyethylamino)-2-hydroxypyrimidine. 2-Hydroxypteridine and aqueous sodium metabisulphite gave sodium 3,4-dihydro-2-hydroxypteridine-4-sulphonate [the orientation follows from the site of addition of water in 2-hydroxypteridine (II)].

## Experimental

Elementary analyses were carried out by the Analytical Section of this Department under Dr. J. E. Fildes. Yields are based on the stage in purification when the substance first gave a single spot in paper chromatography (in both 3% aqueous ammonium chloride and butanol–5N-acetic acid, 7 : 3 v/v), but further purification was carried out before analysis. Ultraviolet spectra were measured on a Perkin–Elmer "Spectracord" instrument and checked on a Hilger "Uvispek" manual instrument. Ionization constants were determined as before.

**3,4-*Dihydro*-2-*hydroxypteridine*.**—(*a*) 2-Hydroxypteridine monohydrate [9] (1·0 g., 0·006 mole) in 0·1N-sodium hydroxide (100 ml.) was hydrogenated at room temperature and pressure over 10% palladium–carbon (0·5 g.) until saturated (20 min.; 1·6 atoms per mole absorbed). The filtrate, adjusted to pH 6, deposited 3,4-*dihydro*-2-*hydroxypteridine* which from water (soluble in 120 parts at 100°, and in 1300 parts at 20°) gave crystals (67%) which darkened at 250° without melting (Found, for material dried at 20°/20 mm.: C, 47·9; H, 4·1; N, 37·2. $C_6H_6N_4O$ requires C, 48·0; H, 4·0; N, 37·3%). It is soluble in cold N (but not 0·1N)-sodium hydroxide, and insoluble in cold dilute mineral acids. Hydrogenation of 2-hydroxypteridine over Raney nickel, in methanol containing one equivalent of sodium hydroxide, gave the same substance (42%).

(*b*) Potassium borohydride (0·33 g.; 8H) was added to 2-hydroxypteridine monohydrate (1 g.) in 0·1N-sodium hydroxide (100 ml.) at 20°. Next day, the suspension was adjusted to pH 7 ($H_3PO_4$), and left at 20° for 1 day. The deposit, recrystallized from water (80 ml.), gave 3,4-dihydro-2-hydroxypteridine (55%) (Found: C, 48·1; H, 4·1; N, 36·9%).

(*c*) To 2-hydroxypteridine monohydrate (1 g.), dissolved in boiling N-sodium carbonate (30 ml.), was added sodium dithionite (4·8 g., 0·024 mole = 8H). The solution became deep orange and deposited white crystals. The suspension (pH 9) was refrigerated overnight and filtered. The crystals were extracted with boiling water (2 × 20 ml.) under carbon dioxide, and the second extract, concentrated to 5 ml., was added to the first. Chilling produced 3,4-dihydro-2-hydroxypteridine (25%) (Found: C, 47·9; H, 4·05; N, 37·1%).

*Deuterium Studies.*—2-Hydroxypteridine monohydrate (1 g.) was reduced with sodium dithionite as above but in heavy water (100% $D_2O$), then recrystallized several times from light water. Combustion of the 4-deutero-3-hydro-2-hydroxypteridine (15·243 mg.) gave 1·03 atoms of deuterium per mole, calculated from the $D_2O$ content of the combustion sample (diluted to 100 mg. with light water) as estimated by infrared spectrophotometry (in a 0·1 mm. quartz cell, interpolating the optical density on a linear graph constructed from densities of 0·1 to 2·0% $D_2O$ in $H_2O$ w/w at 2500 $cm.^{-1}$).[10] When the reduction was carried out in 75% and 50% $D_2O$, only 0·41 and 0·24 atom per mole respectively were found, and hence a large isotope effect is operative.

0·4N-Potassium permanganate (5 ml.) was added dropwise to a stirred suspension of 3,4-dihydro-2-hydroxypteridine (0·15 g.) in 0·02N-potassium hydroxide (150 ml.) at 0°. After 10 min., the mixture was adjusted to pH 6, filtered from manganese dioxide, and evaporated to dryness. Recrystallization of the residue from water gave 2-hydroxypteridine (80%) (Found: C, 43·6; H, 3·8; N, 33·6. Calc. for $C_6H_4N_4O,H_2O$: C, 43·4; H, 3·65; N, 33·7%). This was further oxidized with potassium permanganate as before, and heated for 10 min. at 100° and pH 6 to complete the reaction. The filtrate, treated as before, gave 2,4-dihydroxypteridine (60%), indistinguishable in physical properties from a synthetic sample.[9] When these oxidations were carried out on 4-deutero-3-hydro-2-hydroxypteridine, the 2-hydroxypteridine retained slightly more than half of the deuterium whereas the 2,4-dihydroxypteridine was completely free from deuterium.

Hitherto the combustion of deuterated substances has been carried out in filled tubes.[11] Pteridines, however, burn best in an empty tube at a high temperature. Hence we burned the sample (0·1 to 0·2 mmole) in a Belcher–Ingram "rapid empty-tube" combustion apparatus attached to a vacuum line (a scale drawing is given in Fig. 2; all joints B14). Trap B (27 mm. diam.) was cooled with a carbon dioxide–ethanol bath, and sodium carbonate (5 mg.) was placed in trap C. After complete combustion, additional water was added to the combustion tube to

[9] Albert, Brown, and Cheeseman, *J.*, 1951, 474.
[10] Jones and MacKenzie, *Talanta*, 1960, **3**, 356; Thornton and Condon, *Analyt. Chem.*, 1950, **22**, 690.
[11] Trenner, Arison, and Walker, *Analyt. Chem.*, 1956, **28**, 530.

make 100 mg. in all. By continuing to pass dry oxygen, all the water was collected in B. The tap A was then closed and the apparatus was evacuated to 0·01 mm. The water in B was transferred to C by moving the cooling bath to C. After neutralization, the water was similarly transferred to trap D, which ends in a capillary tube to facilitate transfer to the photometric cell.

*Reduction of 2-Hydroxy-6-methylpteridine.*—2-Hydroxy-6-methylpteridine (0·36 g., see below), reduced with potassium borohydride as was 2-hydroxypteridine (see above), gave *3,4-dihydro-2-hydroxy-6-methylpteridine* (30%) which, recrystallized from water, darkened at 265° without melting (Found: C, 51·3; H, 4·95; N, 34·0. $C_7H_8N_4O$ requires C, 51·2; H, 5·0; N, 34·1%).

*7,8-Dihydro-2-hydroxypteridine.*—Aminoacetal (13·5 g., 0·1 mole) in water (100 ml.) was adjusted to pH 7·5 with acetic acid. Sodium hydrogen carbonate (12 g.) was dissolved in this solution which was added dropwise to a stirred solution of 2,4-dichloro-5-nitropyrimidine [12] (20 g., 0·1 mole) in chloroform (100 ml.). After 3 hours' stirring, the chloroform layer was separated and distilled with N-sodium hydroxide (500 ml.) on a steam bath while nitrogen was bubbled through it for 20 min. The 2-chloro-4-(2,2-diethoxyethylamino)-5-nitropyrimidine

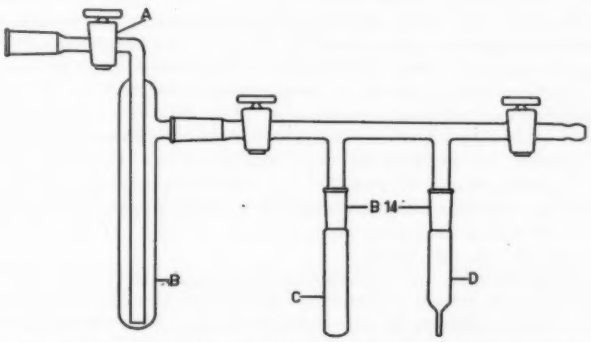



FIG. 2. Apparatus for receiving, purifying, and diluting deuterium oxide after combustion of deuterium-containing substances.

(III) first formed is thus hydrolysed to *4-(2,2-diethoxyethylamino)-2-hydroxy-5-nitropyrimidine* which was isolated in 53% yield by extracting the solution with benzene (3 × 30 ml., set aside), adjusting the aqueous layer to pH 6 (acetic acid), and recrystallizing the precipitate from ethanol to give leaflets, m. p. 157° (Found: C, 44·15; H, 5·9. $C_{10}H_{16}N_4O_5$ requires C, 44·1; H, 5·9%). The benzene layer yielded *2,4-bis-2′-diethoxyethylamino-5-nitropyrimidine*, m. p. 99—100° (Found: C, 49·8; H, 7·3. $C_{16}H_{29}N_5O_6$ requires C, 49·6; H, 7·55%).

4-(2,2-Diethoxyethylamino)-2-hydroxy-5-nitropyrimidine (2·53 g.) in ethanol (300 ml.) was hydrogenated (6H) over Raney nickel at room temperature and pressure. The filtrate was taken to dryness under nitrogen and the residue recrystallized from ethanol–ethyl acetate (1 : 9), giving *5-amino-4-(2,2-diethoxyethylamino)-2-hydroxypyrimidine* (53%), m. p. 174—175° (Found, for substance dried at 20°/0·1 mm.: C, 47·0; H, 7·9; N, 22·1. $C_{10}H_{18}N_4O_3,0{\cdot}75H_2O$ requires C, 46·95; H, 7·7; N, 21·95%). Attempted cyclization gave a complex mixture and hence the following pathway was preferred.

4-2′-Diethoxyethylamino-2-hydroxy-5-nitropyrimidine (14 g.) was refluxed with N-hydrochloric acid (100 ml.) for 20 min. and adjusted to pH 4 with sodium hydrogen carbonate. *2-Hydroxy-4-methylformamido-5-nitropyrimidine* (82%) was filtered off and recrystallized from water. It darkened at 220° without melting (Found: C, 36·5; H, 3·15. $C_6H_6N_4O_4$ requires C, 36·4; H, 3·05%). This substance (2 g.) was hydrogenated over Raney nickel in cold methanol. The catalyst was filtered off and extracted with boiling water (80 ml.), which deposited *7,8-dihydro-2-hydroxypteridine* (23%) which, recrystallized from water, decomposed at 190° without melting (Found, for material dried at 135°/0·1 mm.: C, 47·0; H, 4·1; N, 36·6.

[12] Whittaker, *J.*, 1951, 1565.

$C_8H_8N_4O,0{\cdot}25H_2O$ requires C, 46·6; H, 4·25; N, 36·2%). Further, rather impure, material was obtained from the methanolic filtrate.

*Reduction of* 7,8-*Dihydro*-2-*hydroxypteridine*.—This substance (0·23 g.) was hydrogenated (2H) in 0·05N-acetic acid (50 ml.) over Adams platinum catalyst at 20°. The filtrate was neutralized, and taken to dryness in a vacuum, and the product recrystallized from alcohol to give 5,6,7,8-*tetrahydro*-2-*hydroxypteridine* (70%), decomp. 220° (Found, for material dried at 105°/0·1 mm.: C, 47·5; H, 5·9; N, 36·4. $C_6H_8N_4O$ requires C, 47·35; H, 5·3; N, 36·8%). It absorbed one mole of water from the air in 20 min. at 20°.

*Aminoacetone* (with Dr. F. REICH).—Bromoacetone (66 g.) was added to potassium phthalimide (92 g., 1 equiv.) in dimethylformamide (250 ml.) at 60—70° and kept at this temperature for 1 hr. Water (450 ml.) was added, and the mixture extracted with chloroform (3 × 150 ml.). The chloroform layer was washed with 0·5M-sodium hydroxide, then with water. Evaporation of the chloroform left phthalimidoacetone, m. p. 122°, which was hydrolysed with 7N-hydrochloric acid [13] to aminoacetone hydrochloride, m. p. 81°, in 74% yield based on the bromoacetone.

7,8-*Dihydro*-2-*hydroxy*-6-*methylpteridine*.—4-Acetonylamino-2-chloro-5-nitropyrimidine [8] (6·9 g., 0·03 mole) and sodium acetate trihydrate (6 g., 0·05 mole) were refluxed for 80 min. in acetic acid (100 ml.). The solid which separated on cooling recrystallized from water to give 4-*acetonylamino*-2-*hydroxy*-5-*nitropyrimidine* (36%), m. p. 186° (decomp.) (Found: C, 39·55; H, 3·9. $C_7H_8N_4O_4$ requires C, 39·6; H, 3·8%). This product (2·12 g.) was simultaneously reduced and cyclized by hydrogenation in 90% ethanol (500 ml.) at 50° over Raney nickel (5 g.). The suspension was refrigerated overnight. The catalyst was filtered off and extracted with boiling water (250 ml.) which deposited 7,8-*dihydro*-2-*hydroxy*-6-*methylpteridine* (53%), decomp. ~280° (Found, for material dried at 135°/0·1 mm.: C, 50·95; H, 4·8; N, 34·0. $C_7H_8N_4O$ requires C, 51·2; H, 4·9; N, 34·1%). 7,8-Dihydro-2-hydroxy-4,6-dimethylpteridine,[14] obtained similarly by reducing 4-acetonylamino-2-hydroxy-6-methyl-5-nitropyrimidine,[14] was recrystallized from 250 parts of boiling water (Found: C, 53·8; H, 5·8; N, 31·45. Calc. for $C_8H_{10}N_4O$: C, 53·9; H, 5·8; N, 31·4%).

2-*Hydroxy*-6-*methylpteridine*.—0·1M-Potassium permanganate (20 ml.) was added dropwise with stirring to 7,8-dihydro-2-hydroxy-6-methylpteridine (0·52 g.) in 0·1N-potassium hydroxide (1·1 equiv.) at 0°. The manganese dioxide was filtered off and washed with hot water (10 ml.). The combined filtrate and washings were adjusted to pH 6 with acetic acid and refrigerated overnight. Recrystallization of the precipitate from water gave 2-*hydroxy*-6-*methylpteridine* (67%) decomp. 245° (Found: C, 46·95; H, 4·55; N, 31·3. $C_7H_6N_4O,H_2O$ requires C, 46·7; H, 4·5; N, 31·15%).

4-*Amino*-5-(2,2-*diethoxyethylamino*)-2-*hydroxypyrimidine*.—4,5-Diamino-2-hydroxypyrimidine [15] (0·63 g.) and glyoxal monoacetal [16] (0·85 g., 1 equiv.) in water (25 ml.) were heated for 10 min. on a steam bath. The mixture was taken to dryness under reduced pressure and the residue triturated with acetone (rejected). The solid was hydrogenated in ethanol (50 ml.) over Raney nickel. Concentration of the filtrate gave 4-*amino*-5-(2,2-*diethoxyethylamino*)-2-*hydroxypyrimidine* (10%), m. p. 198—200° (from ethanol) (Found: C, 49·15; H, 7·4; N, 22·7. $C_{10}H_{18}N_4O_3$ requires C, 49·6; H, 7·5; N, 23·1%).

2-*Amino*-3-*hydroxymethylpyrazine*.—To 2-amino-3-methoxycarbonylpyrazine [17] (1·53 g.) in tetrahydrofuran (200 ml.), lithium aluminium hydride (0·38 g.) was added, and the mixture was set aside at 20° for 2 hr. Water (3 ml.) was cautiously added, and the inorganic salts filtered off. The filtrate was taken to dryness and the residue, recrystallized from pentyl acetate, gave 2-*amino*-3-*hydroxymethylpyrazine* (46%), m. p. 118—119·5° (Found, for material dried at 65°/0·1 mm.: C, 47·65; H, 5·7; N, 33·1. $C_5H_7N_3O$ requires C, 48·0; H, 5·65; N, 33·6%). No reaction occurred with hydrobromic acid at 20°, urea at 170°, urethane at 190°, or cyanic acid in water.

Sodium metabisulphite (0·5 g.) was added to a solution of 2-hydroxypteridine monohydrate (0·16 g.) in 0·5N-sodium hydroxide (2 ml.; 1 equiv.). The precipitate obtained on refrigeration gave *sodium* 3,4(?)-*dihydro*-2-*hydroxypteridine*-4(?)-*sulphonate*, needles (from water) (90 mg.),

[13] Ellinger and Goldberg, *J.*, 1949, 263.
[14] Lister and Ramage, *J.*, 1953, 2234.
[15] Brown, *J. Appl. Chem.*, 1957, **7**, 109.
[16] Fischer and Baer, *Helv. Chim. Acta*, 1935, **18**, 514.
[17] Ellingson, Henry, and McDonald, *J. Amer. Chem. Soc.*, 1945, **67**, 1711.

m. p. 310° (decomp.) (Found: C, 27·85; H, 2·4; N, 21·45; S, 12·25. $C_6H_5N_4NaO_4S,0{\cdot}5H_2O$ requires C, 27·6; H, 2·3; N, 21·45; S, 12·3%).

We thank Dr. J. W. Cornforth, F.R.S., and Dr. E. Spinner for helpful discussions. One of us (S. M.) expresses his thanks for an A.N.U. Scholarship.

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## 1017. *Heterocyclic Compounds from Urea Derivatives. Part II.* Synthesis and Cyclisation of 4-Substituted 1-Amidino-semicarbazides and -thiosemicarbazides.*

By Leonard E. A. Godfrey and Frederick Kurzer.

The interaction of aminoguanidine and alkyl or aryl iso(thio)cyanates under various conditions affords 4-substituted 1-amidino(thio)semicarbazides in good yield. Members of the sulphur-containing series are cyclised to 3-alkyl(or -aryl)amino-5-amino-1,3,4-thiadiazoles in acidic media. Their *S*-alkyl derivatives are ring-closed to 3-amino-5-arylamino-1,2,4-triazoles by alkali, and to 4-substituted 3-amino-5-mercapto-1,2,4-triazoles by aniline.

In contrast, 4-substituted 1-amidinosemicarbazides are not cyclised under comparable conditions. They are remarkably stable, being merely acetylated by boiling acetic anhydride or sulphonated by hot concentrated sulphuric acid.

The interaction of aminoguanidine (I) with isocyanate or isothiocyanate esters gives rise either to substituted *N*-aminoamidino(thio)ureas (A; X = O or S) or to 4-substituted 1-amidino(thio)semicarbazides (B; X = O or S), in the presence or absence, respectively, of a blocking group on the hydrazine residue. The synthesis and cyclisation of the former class of compounds (A) has already been described;[1] this paper deals with the corresponding reactions of the series (B).[2]

(A) R·NH·CX·NH·C(:NH)·NH·$NH_2$ $NH_2$·C(:NH)·NH·NH·CX·NHR (B)

The action of phenyl isothiocyanate on aminoguanidine hydrogen carbonate in ethanol was originally shown[3] to result directly, with loss of ammonia, in 3-amino-5-mercapto-4-phenyl-1,2,4-triazole (V; R = Ph). Using aminoguanidine hydrochloride, Fry and Lambie[4] recently obtained a series of 4-substituted 1-amidinothiosemicarbazides (B; X = S), which are obviously concerned as intermediates in the above reaction, and demonstrated[5] their ready cyclisation in alkaline media to 4-substituted 3-amino-5-mercapto-1,2,4-triazoles (V). The corresponding reactions of isocyanate esters, however, have apparently not been studied.

In the present work, the condensation under various conditions of aminoguanidine salts and isothiocyanate esters was first re-examined. Fry and Lambie's procedure[4] afforded 4-substituted 1-amidinothiosemicarbazides (II) in satisfactory yields which were however improved, in the aliphatic series, by extending the time of reaction and by use of triethylamine as catalyst. In the preparation of aromatic homologues, nevertheless, prolonged heating was inadmissible, since increasing proportions of triazole (V) were

* Part I, *J.*, 1960, 3437.

[1] Godfrey and Kurzer, *J.*, 1960, 3437.

[2] For a preliminary account of part of this work, see Kurzer and Godfrey, *Chem. and Ind.*, 1961, 107.

[3] Fantl and Silbermann, *Annalen*, 1928, **467**, 274.

[4] Fry and Lambie, B.P. 741,280/1955.

[5] Fry and Lambie, B.P. 741,228/1955.

formed, showing that under suitable conditions, the cyclisation (II ⟶ V) may also proceed in other than alkaline media. In this, as in the other variations of this method, it was advantageous to isolate the products as the sparingly soluble, highly crystalline toluene-*p*-sulphonates.

Condensation of the compounds in aqueous-ethanolic alkali, that has been successful in the synthesis of *N*-substituted *N'*-benzimidoylthioureas [6] R'·NH·CS·NH·CR:NH, gave only moderate yields of the aromatic homologues (II; R = Ph or *p*-$C_6H_4Me$). The use of ethanolic sodium ethoxide, in the aliphatic series, resulted exclusively in cyclisation to the substituted triazoles (V).

When dimethylformamide was used as solvent reaction of aminoguanidine with isothiocyanate or isocyanate esters was smoother and much faster and there were no side reactions. 1-Amidino-4-phenylthiosemicarbazide (II; R = Ph), for example, was obtained in 82% yield at 100° in 30 min. As expected, the less reactive [7] alkyl isothiocyanates required an extended time of reaction to produce comparable results.

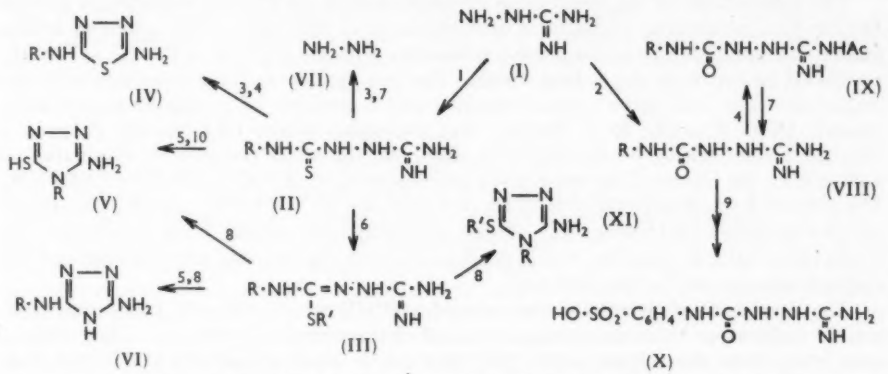
Attempts to condense aminoguanidine salts and isocyanates, for which procedures involving aqueous or alcoholic media are inapplicable, were first made in anhydrous pyridine. Yields were low, however, and much carbanilide was produced. Here, the use of dimethylformamide as solvent proved indispensable, affording the new 4-substituted 1-amidino semicarbazides (VIII) rapidly and in excellent yield. The remarkable power of this solvent of accelerating the present addition reactions may be ascribed, as in numerous other examples,[8] to its high dielectric constant (ε 36·7,[9] compared with ε 12·4 for pyridine, both at 25°) and to the possible formation of highly reactive intermediate addition complexes. The existence of a variety of addition compounds of dimethylformamide is well established; [10] also complexes of aniline or carbanilide with stannous chloride have superior reactivity towards phenyl isocyanate [11] in a comparable synthesis.

4-Substituted 1-amidinothiosemicarbazides (II) are monoacid bases; they were isolated as stable salts only, since cyclisation to 4-substituted 3-amino-5-mercapto-1,2,4-triazoles (V) occurred when attempts were made to liberate the free bases even by dilute ammonia at 0°. They were desulphurised and decomposed, with evolution of isocyanides, by sodium plumbite in the presence of alkali. Their monopicrates were unusually soluble and difficult to crystallise. The 4-substituted 1-amidinothiosemicarbazides (II) were readily converted into their *S*-benzyl-derivatives (as III), which were isolated without difficulty as free bases in the presence of strong alkalis. Since compounds (II) and (III) differ structurally merely in their mercapto- and benzylmercapto-group, neither of which is concerned in the ring-closure to (V) or (XI), it is noteworthy that only the former compounds are rapidly cyclised by cold alkalis; steric hindrance (in III) may contribute to their resistance to cyclisation (to XI) under mild conditions (see also below).

Three distinct cyclisations of 4-substituted 1-amidinothiosemicarbazides (II) are theoretically feasible: Two alternative modes of elimination of ammonia, between the amidino- and the alkyl(or aryl)amino- or thiol groups (in II), respectively, give rise to either triazoles (V) or thiadiazoles (IV), while loss of hydrogen sulphide produces 1,2,4-triazoles (VI). The first ring-closure, occurring in basic media, is well established.[3,5] Cyclisations of the second type have recently been observed [12] for the closely related

[6] Pinner, *Ber.*, 1899, **22**, 1600; Kurzer and Tertiuk, *J.*, 1959, 2851.
[7] Orndorff and Richmond, *Amer. Chem. J.*, 1899, **22**, 458; Slotta, Tschesche, and Dressler, *Ber.*, 1930, **63**, 208.
[8] (*a*) Ross and Labes, *J. Amer. Chem. Soc.*, 1957, **79**, 4155; (*b*) Hartman, *Nature*, 1955, **176**, 1024; Blume and Swezey, *TAPPI*, 1954, **37**, 481; (*c*) Kornblum *et al.*, *J. Amer. Chem. Soc.*, 1956, **78**, 1497; Joly, Warnant, and Nominé, *Bull. Soc. chim. France*, 1957, 330; Bunnet and Conner, *J. Org. Chem.*, 1958, **23**, 305; (*d*) Kornblum and Kendall, *J. Amer. Chem. Soc.*, 1952, **74**, 5782.
[9] Leader and Gormley, *J. Amer. Chem. Soc.*, 1951, **73**, 5731.
[10] Haszeldine, *J.*, 1954, 4145; Hall, *J. Amer. Chem. Soc.*, 1956, **78**, 2717; Jaunin, *Helv. Chim. Acta*, 1956, **39**, 111.
[11] Baker and Holdsworth, *J.*, 1945, 724.
[12] Kurzer, *J.*, 1961, 1617.

thiobenzamidoguanidines (D) which are converted by hydrochloric acid or acetic anhydride into 5-substituted 2-amino-1,3,4-thiadiazoles or their acetyl derivatives. In the present work, hydrochloric acid proved unsuitable, degrading the reactants (*e.g.*, II; R = Ph) directly to phenyl isothiocyanate and hydrazine. 3-Amino-5-anilino-1,3,4-thiadiazole



Reagents: 1, PhNCS. 2, PhNCO. 3, $H_3PO_4$. 4, $Ac_2O$. 5, NaOH. 6, R'Cl–NaOH. 7, HCl. 8, Ph·$NH_2$. 9, $H_2SO_4$. 10, Aq. $NH_3$.

was not formed intermediately, since its stability in boiling concentrated hydrochloric acid was separately established.

The desired cyclisation occurred in 100% orthophosphoric acid at 120—130°, affording 2-amino-5-alkyl(or -aryl)amino-1,3,4-thiadiazoles (IV) in satisfactory yields. Feeble evolution of hydrogen sulphide indicated the loss of small quantities of reactant in side reactions. The methyl homologue (II; R = Me) reacted anomalously, however, being completely decomposed to hydrazine by this reagent also. The familiar ring-closure of 1-acylthiosemicarbazides to 2-amino-5-alkyl(or -aryl)-1,3,4-thiadiazoles by orthophosphoric acid [13] differs from the present reaction in that water instead of ammonia is eliminated, and illustrates the preferential formation of the 1,3,4-thiadiazole over that of the 1,3,4-oxadiazole ring-system under these conditions.

Acetic anhydride at its boiling point effected the same cyclisation, yielding 1,3,4-thiadiazoles (IV) as the diacetyl derivatives, which were converted into their parent compounds (IV) by acid hydrolysis. The present cyclisation, by phosphoric acid or acetic anhydride, resembles the ring-closures of the comparable oxygen- and sulphur-containing compounds: both types of compound (C; X = O) [14,15] and (C; X = S) [14,16] are cyclised to the appropriate 1,3,4-thiadiazoles in acid media, but the latter reaction differs from the synthesis now described in proceeding with loss (from C; X = S, R = Ph) of both ammonia and hydrogen sulphide simultaneously to yield 2-mercapto- and 2-amino-5-anilino-1,3,4-thiadiazoles side by side.

(C) $NH_2$·CX·NH·NH·CS·NHR  $NH_2$·C(:NH)·NH·NH·CSR (D)

The third type of ring closure (II ⟶ VI), attended by loss of hydrogen sulphide, was achieved indirectly on treatment of the *S*-benzyl derivatives (III) with boiling alkali. 1-Amidino-*S*-benzyl-4-phenylisothiosemicarbazide (III; R = Ph, R' = Ph·$CH_2$), for example, was converted into 3-amino-5-anilino-1,2,4-triazole (VI; R = Ph) in 78% yield. The free

[13] Hoggarth, *J.*, 1949, 1166.
[14] Guha, *J. Amer. Chem. Soc.*, 1923, **45**, 1041.
[15] Arndt, Milde, and Tschenscher, *Ber.*, 1922, **55**, 341.
[16] Freund, *Ber.*, 1894, **27**, 1774; 1895, **28**, 946; Busch and Schmidt, *Ber.*, 1913, **46**, 2240; Busch and Lotz, *J. prakt. Chem.*, 1914, **90**, 257; for summary cf. Bambas, "The Chemistry of Heterocyclic Compounds," Interscience Publ. Inc., New York, 1952, Vol. IV, p. 124 *et seq.*

thiol group (of II) is presumably stabilised in alkaline media by salt-formation, with consequent preferential elimination of ammonia and production of (V); the *S*-alkylated thiol group (of III), on the other hand, being removed as a whole by alkalis in the familiar manner,[17] provides the conditions for ring-closure to diaminotriazoles (VI).

The replacement of the *S*-alkylthio- by amino-groups (in III) was expected to provide further data concerning cyclisations of compounds of this type. The action of boiling aniline on 1-amidino-*S*-benzyl-4-phenylisothiosemicarbazide (III; R = Ph, R′ = Ph·$CH_2$) proceeded in two ways depending whether the free base or its toluene-*p*-sulphonate was employed. The base gave approximately equal quantities of 3-amino-5-benzylthio-4-phenyl- (XI; R = Ph, R′ = Ph·$CH_2$) and 3-amino-5-anilino-1,2,4-triazole (VI; R = Ph), the former arising by direct loss of ammonia, the latter possibly by elimination of aniline from the intermediate substituted aminoguanidine, $(Ph{\cdot}NH)_2C{:}N{\cdot}NH{\cdot}C(:NH){\cdot}NH_2$. The toluene-*p*-sulphonate (III; R = Ph or *p*-$C_6H_4Me$, R′ = Ph·$CH_2$) afforded 3-amino-4-aryl-5-mercapto-1,2,4-triazoles (V) almost quantitatively; under these conditions, the *S*-alkyl derivative is therefore merely dealkylated, and the resulting parent compound (II) cyclised subsequently in the usual way.

The 4-substituted 1-amidinosemicarbazides (VIII) were monoacid bases that were readily isolated as toluene-*p*-sulphonates and characterised as picrates. They differed completely from the sulphur series (II), however, in their remarkable stability in acid media. Thus, 1-amidino-4-phenylsemicarbazide (VIII; R = Ph), on treatment with acetic anhydride at 120°, gave merely an acetyl derivative (probably IX), which was reconverted into the parent base by acid hydrolysis. Attempts to cyclise 1-amidino-4-phenylsemicarbazide with simultaneous dehydration (*i.e.*, to VI) by concentrated sulphuric acid gave only 1-amino-4-*p*-sulphophenylsemicarbazide (X), the structure of which was established by its degradation to sulphanilic acid.

The rapid ring-closure of 4-substituted 1-amidinothiosemicarbazides in alkaline media (to V) is also without parallel in the oxygen series: a model compound (VIII; R = Ph) was mostly recovered after brief heating with alkali, but was degraded to aniline on distillation. In their failure to undergo cyclisation, 4-substituted 1-amidinosemicarbazides thus differ, not only from their sulphur analogues, but also from the closely related acylaminoguanidines, $R{\cdot}CO{\cdot}NH{\cdot}NH{\cdot}C(:NH){\cdot}NH_2$, which are converted into 5-substituted 3-amino-1,2,4-triazoles with great ease.[18]

The new ring-closures of 4-substituted 1-amidinothiosemicarbazides now described provide further examples of the usefulness of aminoguanidine as a starting material in heterocyclic syntheses; in general, the observed formation of 1,3,4-thiadiazoles and 1,2,4-triazoles fits into the known pattern of the reactions of substituted thiosemicarbazides under comparable conditions.

## Experimental

Light petroleum had b. p. 60—80°. Dimethylformamide used as solvent was redistilled before use, and the water-containing fore-run rejected. Ultraviolet absorption measurements were made with a Unicam S.P. 500 spectrophotometer and 0·00005M-ethanolic solutions.

Aminoguanidine picrate was prepared from the sulphate monohydrate (0·66 g., 0·005 mole) in water (5 ml.) and 0·05M-picric acid (100 ml., 0·005 mole) at room temperature; the yellow precipitate gave deep yellow prisms, m. p. 182—185° (decomp.) (from 90% ethanol) (Found: C, 27·9; H, 3·0. $CH_6N_4{\cdot}C_6H_3N_3O_7$ requires C, 27·7; H, 3·0%). Thiele [19] prepared this salt but gave no m. p.

*Aminoguanidine Toluene-*p*-sulphonate.*—Aminoguanidine sulphate monohydrate (1·32 g., 0·01 mole) in water (5 ml.), treated with toluene-*p*-sulphonic acid monohydrate (2·85 g.,

[17] Arndt, *Ber.*, 1921, **54**, 2238.
[18] Thiele and Heidenreich, *Ber.*, 1893, **26**, 2598; Thiele and Manchot, *Annalen*, 1898, **313**, 33; Hoggarth, *J.*, 1950, 612.
[19] Thiele, *Annalen*, 1892, **270**, 1.

0·015 mole) in water (5 ml.), gave crystals (2·0 g., 80%), which gave, on crystallisation from water (5 ml. per g.), prisms of the *toluene*-p-*sulphonate*, m. p. 203—205° (decomp.) (Found: C, 38·9; H, 5·75. $CH_6N_4,C_7H_8O_3S$ requires C, 39·0; H, 5·7%).

*Hydrazine Dipicrate.*—10% Aqueous hydrazine hydrate (1 ml., 0·002 mole) added to 0·05M-picric acid (100 ml., 0·005 mole) gave a clear solution, which on treatment with ammonium chloride (20 g.) rapidly deposited yellow needles. They were collected at 0°, washed with very little water, and crystallised from ethanol (40 ml. per g.; recovery 60—70%) or water (10 ml. per g.), giving needles of *hydrazine dipicrate*, m. p. 289—292° (decomp., after darkening from 270°), almost quantitatively (Found: C, 29·7; H, 2·3; N, 23·3. $N_2H_4,2C_6H_3N_3O_7$ requires C, 29·4; H, 2·0; N, 22·9%).

*Thiosemicarbazide Series*

*Preparation of* 1-*Amidino*-4-*phenylthiosemicarbazide.*—(*a*) A solution of aminoguanidine sulphate monohydrate (5·8 g., 0·044 mole) in water (20 ml.) was treated with phenyl isothiocyanate (5·4 g., 0·04 mole), followed by 3N-aqueous sodium hydroxide (13·3 ml., 0·04 mole) and ethanol (20 ml.), so that a one-phase system was obtained. The orange-brown warm mixture was stirred at room temperature during 2 hr., a little more ethanol being added if necessary to prevent separation into two phases. The solution was set aside overnight, a trace of solid removed, and the orange filtrate treated with toluene-*p*-sulphonic acid monohydrate (11·4 g., 0·06 mole). The resulting solid was collected at 0° (9·5—11 g.) and crystallised from ethanol–water (4 and 1 ml. per g.): prisms (filtrate: F) of solvated 1-*amidino*-4-*phenylthiosemicarbazide toluene*-p-*sulphonate*, m. p. 133—135° (decomp.), were obtained (7·5—8·5 g., 44—50%). A specimen, crystallised twice more from ethanol (25 ml. per g.), had m. p. 134—136° (decomp.) (Found: C, 47·5; H, 5·5; N, 16·3; S, 15·0. $C_8H_{11}N_5S,C_7H_8O_3S,C_2H_5{\cdot}OH$ requires C, 47·8; H, 5·85; N, 16·4; S, 15·0%). It rapidly gave lead sulphide and phenyl isocyanide with hot alkaline sodium plumbite.

The free base was not isolated, since cyclisation to 3-amino-5-mercapto-4-phenyl-1,2,4-triazole occurred on treatment of the toluene-*p*-sulphonate at 0° with such weak bases as ammonia (see below).

Filtrate F, on dilution with an equal volume of ether, gave a white solid which consisted, after crystallisation from 90% ethanol, of aminoguanidine toluene-*p*-sulphonate (0·85 g., 8%), m. p. and mixed m. p. 202—204° (decomp.) (Found: C, 39·2; H, 5·7; N, 23·0; S, 13·35. Calc. for $CH_6N_4,C_7H_8O_3S$: C, 39·0; H, 5·7; N, 22·8; S, 13·0%).

(*b*) Finely powdered aminoguanidine hydrochloride (2·2 g., 0·02 mole) in dimethylformamide (5 ml.) was treated with phenyl isothiocyanate (2·70 g., 0·02 mole) and kept at 100° during 30 min., complete dissolution occurring after 10—15 min. The liquid, stirred into water (40 ml.) and treated with toluene-*p*-sulphonic acid monohydrate (4·75 g., 0·025 mole) in water (10 ml.), gave solvated 1-amidino-4-phenylthiosemicarbazide toluene-*p*-sulphonate, m. p. and mixed m. p. 134—136° (decomp.) (6·4—6·8 g., 75—82%; from 80% ethanol).

(*c*) The hydrochloride, obtained by Fry and Lambie's procedure [4] in 50—60% yield, formed white crystals, m. p. 172—174° (decomp.) (from ethanol–light petroleum). Fry and Lambie [4] give m. p. 177—180°. More prolonged boiling (10 or 20 hr.) resulted in partial cyclisation to 3-amino-5-mercapto-4-phenyl-1,2,4-triazole, m. p. and mixed m. p. (see below) 264—266° (decomp.) (15—30%, respectively); this separated directly from the reaction mixture on cooling; the filtrate therefrom, after the usual treatment, gave the above hydrochloride in ~45 and 30% yield, respectively.

A solution of the solvated toluene-*p*-sulphonate (0·002 mole) in warm water (30 ml.), treated with 2N-ammonia (1 ml., 0·002 mole) and 0·05M-picric acid (40 ml., 0·002 mole), slowly deposited a yellow powder at 0°. The product (0·57 g., 65%) formed yellow prisms of the *picrate*, m. p. 180—182° (decomp., somewhat subject to the rate of heating) (from ethanol) (Found: C, 38·0; H, 3·3. $C_8H_{11}N_5S,C_6H_3N_3O_7$ requires C, 38·4; H, 3·2%).

*Reactions of* 1-*Amidino*-4-*phenylthiosemicarbazide.*—(a) *With phosphoric acid.* A solution of the solvated toluene-*p*-sulphonate (4·27 g., 0·01 mole) in 100% orthophosphoric acid (30 ml.) was kept at 120° during 1 hr. The pale pink liquid was stirred into concentrated aqueous ammonia (60 ml.)–ice (100 g.), and the crystalline precipitate collected after 12 hr. at 0° (1·5 g.). The product gave prisms from ethanol (20 ml.)–light petroleum (40 ml.) or platelets from water (100 ml. per g.) of 2-amino-5-anilino-1,3,4-thiadiazole, m. p. 204—206° (1·06—1·30 g., 56—68%)

(lit., m. p. 205° [20] or 215° [14]) (Found: C, 50·1; H, 4·3; N, 29·9. Calc. for $C_8H_8N_4S$: C, 50·0; H, 4·2; N, 29·2%).

1-Amidino-4-phenylthiosemicarbazide hydrochloride [4] was cyclised under the same conditions (with evolution of hydrogen chloride) to 2-amino-5-anilino-1,3,4-thiadiazole in 60% yield.

The picrate formed yellow needles, m. p. 225—228° (decomp.) (Guha [11] gives m. p. 226°) (Found: C, 41·65; H, 3·2. Calc. for $C_8H_8N_4S,C_6H_3N_3O_7,C_2H_5{\cdot}OH$: C, 41·1; H, 3·6%). The *toluene*-p-*sulphonate*, obtained nearly quantitatively from the thiadiazole and toluene-*p*-sulphonic acid (100% excess) in the minimum volume of boiling water, consisted of needles, m. p. 268—269° (decomp. after sintering at 262°) (from ethanol, 100 ml. per g.) (Found: C, 49·6; H, 4·4; N, 14·1; S, 16·0. $C_8H_8N_4S,C_7H_8O_3S,C_2H_5{\cdot}OH$ requres C, 49·8; H, 5·4; N, 13·7; S, 15·6%). The diacetyl derivative, obtained on boiling the thiadiazole (0·001 mole) in acetic anhydride (4 ml.) during 30 min., formed prisms (65%), m. p. 274—276° (decomp., after shrinking at 270°) (from ethanol). Fromm and Jokl [20] give m. p. 264°.

(b) *With acetic anhydride.* The solvated toluene-*p*-sulphonate (2·14 g., 0·005 mole) in acetic anhydride (20 ml.) was refluxed during 20 min., then added to water (80 ml.). The separated solid (0·76 g., 55%) gave, on crystallisation from ethanol (carbon), needles of the diacetyl derivative of 2-amino-5-anilino-1,3,4-thiadiazole, m. p. [and mixed m. p. with the derivative obtaind in (a), above] 274—276° (after shrinking at 270°) (Found: C, 51·9; H, 4·4; N, 20·7; S, 11·8. Calc. for $C_{12}H_{12}N_4O_2S$: C, 52·2; H, 4·35; N, 20·3; S, 11·6%).

(c) *With hydrochloric acid.* The thiosemicarbazide (2·14 g., 0·005 mole) in concentrated hydrochloric acid (10 ml.) was refluxed during 30 min. There was slight evolution of hydrogen sulphide, and oily drops in the refluxing liquid smelled of phenyl isothiocyanate. The clear solution, set aside in an evaporation basin overnight, deposited crystals (0·86 g., 40%) of recovered reactant (m. p. and mixed m. p. 131—135°, from ethanol). The acidic filtrate therefrom, nearly neutralised by concentrated aqueous ammonia and treated with picric acid, slowly deposited a yellow precipitate (1·22—1·45 g., 50—60%) of hydrazine dipicrate, m. p. and mixed m. p. 288—292° (decomp., after darkening from 270°) (from 95% ethanol) (Found: C, 29·4; H, 2·7; N, 23·0%). The use of 3N-hydrochloric acid resulted in 65% recovery of the reactant, and 20—30% yields of hydrazine dipicrate. 2-Amino-5-anilino-1,3,4-thiadiazole (0·005 mole) was substantially recovered after its solution in concentrated hydrochloric acid (10 ml.) had been boiled during 30 min.

(d) *With alkali.* The reactant (0·005 mole), on being refluxed with 3N-sodium hydroxide (10 ml., 0·03 mole) during 30 min., gave an intensely yellow and later colourless solution, while ammonia was evolved. Acidification with 3N-hydrochloric acid gave crystals (0·86 g., 90%) of 3-amino-5-mercapto-4-phenyl-1,2,4-triazole, m. p. 264—266° (decomp.) (from water) (Found: C, 45·95; H, 4·8. Calc. for $C_8H_8N_4S,H_2O$: C, 45·7; H, 4·8%). $\lambda_{min.}$ 237 (log ε 3·75); $\lambda_{max.}$ 265 mμ (log ε 3·93). The m. p. is variously given between 260° and 268° in the literature.[3,5,15,20–22]

(e) *With ammonia.* A solution of the toluene-*p*-sulphonate (0·005 mole) in 6N-ammonia (15 ml.) at 0° during 2 days deposited crystals (0·74 g., 77%) of the same triazole, m. p. and mixed m. p. 264—266° (decomp.) (from ethanol). The ammoniacal filtrate, on being boiled during 5 min., gave a further crop (12%) of the triazole on subsequent storage at 0°.

1-*Amidino*-4-p-*tolylthiosemicarbazide.*—(*a*) To a solution of aminoguanidine sulphate monohydrate (2·90 g., 0·022 mole) in water (10 ml.) were added successively *p*-tolyl isothiocyanate (3·0 g., 0·02 mole), 3N-sodium hydroxide (6·7 ml., 0·02 mole), and ethanol (30 ml.). The resulting suspension was stirred at room temperature during 6 hr., further ethanol (10 ml.) being added after 1 hr.; after a further 72 hr., water (20 ml.) was added, inorganic material (1·5—2 g.) removed, and the filtrate treated with toluene-*p*-sulphonic acid monohydrate (7·60 g., 0·04 mole). The separated crystals (4—4·5 g.), when recrystallised from ethanol (15 ml. per g., recovery 80%), then water (20 ml. per g., recovery 60%), formed granules of the *toluene*-p-*sulphonate*, m. p. 160—162° (decomp., dependent on the rate of heating) (2·2—2·8 g., 28—

[20] Fromm and Jokl, *Monatsh.*, 1923, **44**, 303.

[21] Mazurewich, (*a*) *Bull. Soc. chim. France*, 1927, **41**, 644, 648; 1930, **47**, 1163, 1176; *J. Russ. Phys. Chem. Soc.*, 1927, **59**, 34; 1930, **62**, 1141, 1155; (*b*) *Bull. Soc. chim. France*, 1927, **41**, 659; *J. Russ. Phys. Chem. Soc.*, 1927, **59**, 61; see also *Univ. État Kiev, Bull. sci. Rec. chim.*, 1935, **1**, No. 4, 9 (*Chem. Abs.*, 1936, **30**, 7574).

[22] Guha and Mehta, *J. Indian Inst. Sci.*, 1938, **21**, *A*, 41, 53.

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36%) (Found: C, 49·1; H, 5·0; N, 17·25. $C_9H_{13}N_5S_2C_7H_8O_3S$ requires C, 48·6; H, 5·3; N, 17·7%). It gave lead sulphide, and a strong smell of isocyanide, with boiling alkaline sodium plumbite.

(*b*) Interaction of aminoguanidine hydrochloride and *p*-tolyl isothiocyanate (0·02 mole each) in dimethylformamide (5 ml.) at 100° during 1 hr., followed by addition of the liquid to water (40 ml.), gave a white solid which was collected at 0° (4·25 g., 77%) (filtrate: T). Crystallisation from 90% ethanol (10 ml. per g.) gave needles of the *hydrochloride monohydrate*, m. p. 195—197° (decomp.) (Found: C, 38·2; H, 5·5; N, 25·0; Cl, 12·3. $C_9H_{13}N_5S,HCl,H_2O$ requires C, 38·9; H, 5·8; N, 25·2; Cl, 12·8%). A further quantity (up to 20%) of the compound was isolated from filtrate T as the toluene-*p*-sulphonate.

(*c*) Interaction of the same reactants (0·02 mole each) in boiling ethanol (20 ml.) during 4 hr. gave, after several days' storage, the hydrochloride (3·60 g., 65%), m. p. and mixed m. p. (see *b*, above) 194—196° (decomp.). A litte more material was isolated from the filtrates as the toluene-*p*-sulphonate (5%). More prolonged refluxing resulted solely in partial cyclisation (15%) to 3-amino-5-mercapto-4-*p*-tolyl-1,2,4-triazole (cf. below).

Addition of picric acid (0·115 g., 0·0005 mole) in ethanol (3 ml.) to a solution of the hydrated hydrochloride (0·14 g., 0·0005 mole) in boiling ethanol (12 ml.), followed by dilution with ether (20 ml.), gave a liquid which slowly deposited yellow prisms (0·06 g., 25%) and a white powder. Slow crystallisation of the former (hand-picked) from ethanol (5 ml.) gave the *picrate*, m. p. 175—177° (decomp.) (Found: C, 41·1; H, 4·3. $C_9H_{13}N_5S,C_6H_3N_3O_7,C_2H_5{\cdot}OH$ requires C, 41·0; H, 4·4%). Attempts to convert the toluene-*p*-sulphonate into this picrate, in the presence or absence of ammonia, failed, because of its unusually high solubility, the reactant being largely recovered.

(*d*) Treatment of the toluene-*p*-sulphonate (1·0 g., 0·0025 mole) with orthophosphoric acid and isolation of the product as described above for the phenyl homologue gave plates (0·23 g., 45%) of 2-amino-5-*p*-toluidino-1,3,4-thiadiazole, m. p. 205—206° (once from water, once from ethanol–light petroleum [carbon]) (Guha and Mehta [22] give m. p. 203°) (Found: C, 53·0; H, 4·9; N, 27·3; S, 15·35. Calc. for $C_9H_{10}N_4S$: C, 52·4; H, 4·85; N, 27·2; S, 15·5%).

(*e*) Treatment of the toluene-*p*-sulphonate (0·005 mole) with alkali as described for the phenyl homologue gave (0·77 g., 75%) 3-amino-5-mercapto-4-*p*-tolyl-1,2,4-triazole, m. p. 278—280° (prisms from ethanol) (Found: C, 52·2; H, 4·7. Calc. for $C_9H_{10}N_4S$: C, 52·4; H, 4·85%). It had $\lambda_{min.}$ 241 (log ε 3·78), $\lambda_{max.}$ 268 mμ (log ε 3·96). The m. p. is variously given between 272° and 277° in the literature.[21b,22]

*Preparation of* 1-*Amidino-4-methylthiosemicarbazide*.—(*a*) Interaction of aminoguanidine hydrochloride and methyl isothiocyanate (0·02 mole each) in dimethylformamide (6 ml.) at 100° during 3 hr., followed by dilution with water (25 ml.) and treatment with toluene-*p*-sulphonic acid (0·024 mole), gave, on storage at 0° and subsequent spontaneous evaporation of the filtrates, two successive crops of the *toluene*-p-*sulphonate*, (4·1 g., 64%), forming prisms, m. p. 205—207° (decomp.) (from ethanol; 30 ml. per g.) (Found: C, 37·6; H, 5·3. $C_3H_9N_5S,C_7H_8O_3S$ requires C, 37·6; H, 5·3%). The same salt (80%), m. p. and mixed m. p. 205—207° (decomp.), resulted from equimolecular quantities (0·002 mole) of the hydrochloride (see *b*, below) and toluene-*p*-sulphonic acid in water (8 ml.).

(*b*) The hydrochloride was prepared by Fry and Lambie's procedure,[4] but with addition of a little triethylamine as catalyst, in 50—72% yield, after 20—50 hours' refluxing. Crystallised from 85% ethanol (25 ml. per g., recovery 50%), it formed prisms, m. p. 220—222°, (decomp.) (Found: C, 19·9; H, 5·4. Calc. for $C_3H_9N_5S,HCl$: C, 19·6; H, 5·45%). Fry and Lambie [4] give m. p. 209—210° (from water). Solutions of the product slowly gave a black precipitate with boiling alkaline sodium plumbite.

The *picrate*, prepared from the hydrochloride in 80% ethanol, formed yellow needles (70%), m. p. 212—214° (decomp.) (from 90% ethanol) (Found: C, 28·85; H, 3·1. $C_3H_9N_5S,C_6H_3N_3O_7$ requires C, 28·7; H, 3·2%).

(*c*) A suspension of aminoguanidine sulphate monohydrate (7·25 g., 0·055 mole) in a solution from sodium (1·15 g., 0·05 g.-atom) in ethanol (80 ml.) was stirred during 30 min. After addition of methyl isothiocyanate (3·65 g., 0·05 mole), the stirred mixture was kept at room temperature during 15 min. and refluxed during 1 hr. Most of the ethanol was removed in a vacuum, the residual liquid stirred into water (50 ml.), and the acidity adjusted to pH 6·5 with concentrated hydrochloric acid. The product, collected at 0° (3·3 g., 51%) and crystallised from water (25 ml. per g., recovery 75%), consisted of needles of 3-amino-5-mercapto-4-methyl-1,2,4-triazole,

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m. p. 267—269° (Fry and Lambie [5] give m. p. 269—272°) (Found: C, 28·0; H, 4·6; N, 43·2; S, 24·95. Calc. for $C_3H_6N_4S$: C, 27·7; H, 4·6; N, 43·1; S, 24·6%), $\lambda_{min.}$ 228 (log ε 3·52), $\lambda_{max.}$ 260 mμ (log ε 4·14).

Aminoguanidine sulphate monohydrate, suspended in pyridine, failed to react with methyl isothiocyanate at 100° during 4 hr.

*3-Amino-5-p-chlorobenzylthio-4-methyl-1,2,4-triazole.*—A solution of the foregoing triazole (0·65 g., 0·005 mole) and 4-chlorobenzyl chloride (0·97 g., 0·006 mole) in ethanol (10 ml.), treated with N-sodium hydroxide (5 ml., 0·005 mole), was kept at 100° during 15 min., then diluted with water (20 ml.). The solid (1·2 g.), collected at 0°, crystallised from benzene–ethanol (3 : 1) as plates of the *p-chlorobenzylthio-derivative*, m. p. 165—167° (Found: C, 47·4; H, 4·3. $C_{10}H_{11}ClN_4S$ requires C, 47·2; H, 4·3%).

*Reactions of 1-Amidino-4-methylthiosemicarbazide.*—(a) *Action of phosphoric acid.* A solution of the hydrochloride (0·92 g., 0·005 mole) in 100% orthophosphoric acid (10 ml.) was kept at 120° during 30 min. (slight evolution of hydrogen chloride), added to ice (40 g.) and ammonia (*d* 0·88; 20 ml.), and acidified (to pH 6) with 3N-acetic acid (slight odour of hydrogen sulphide). Addition of 0·075M-picric acid (100 ml., 0·0075 mole) slowly gave hydrazine dipicrate (1·57 g., 64%), m. p. and mixed m. p. 288—290° (decomp., after darkening from 260—270°) (Found: C, 30·0; H, 2·4; N, 22·8%).

(b) *Action of acetic anhydride.* The hydrochloride (1·83 g., 0·01 mole) was refluxed in acetic anhydride (20 ml.) during 1 hr., but complete solution did not occur. The resulting needles were collected at 0°; addition of the filtrate to water gave a little more product (total, 1·18 g., 55%). Crystallised from methanol (120 ml. per g.), it consisted of the *diacetyl derivative* of 2-amino-5-methylamino-1,3,4-thiadiazole, m. p. 319—320° (Found: C, 40·1; H, 5·2; N, 25·6; S, 14·6. $C_7H_{10}N_4O_2S$ requires C, 39·25; H, 4·7; N, 26·2; S, 14·95%).

The diacetyl derivative (1·07 g., 0·005 mole) was refluxed with 3N-hydrochloric acid (5 ml.) during 30 min., the solution neutralised with 3N-ammonia, and the filtered liquid treated with 0·05M-aqueous picric acid (100 ml., 0·005 mole). The yellow precipitate (1·53 g., 85%) was *2-amino-5-methylamino-1,3,4-thiadiazole picrate*, m. p. 218—221° (decomp., darkening from 210°) (from 80% ethanol) (Found: C, 30·9; H, 2·7. $C_3H_6N_4S,C_6H_3N_3O_7$ requires C, 30·1; H, 2·5%).

Attempts to isolate the thiadiazole as the base or the toluene-*p*-sulphonate from the hydrolysate were unsuccessful, because of the high solubility of these compounds in water.

*1-Amidino-4-n-butylthiosemicarbazide.*—(*a*) Interaction of aminoguanidine hydrochloride and butyl isothiocyanate (0·03 mole each) in dimethylformamide (8 ml.) at 100° during 3 hr., dilution with water (40 ml.), and addition of toluene-*p*-sulphonic acid (0·035 mole) gave the toluene-*p*-sulphonate monohydrate (9·1 g., 80%), m. p. and mixed m. p. (see below) 160—163° (decomp.) (from water). It gave lead sulphide and isocyanide with boiling basified sodium plumbite.

(*b*) A solution of powdered aminoguanidine hydrochloride (5·53 g., 0·05 mole), butyl isothiocyanate (5·75 g., 0·05 mole), and triethylamine (0·1 ml.) in ethanol (100 ml.) was refluxed during 48 hr., then distilled to small volume (20 ml.). The separated product (1·5—2 g.), collected at room temperature, was recovered aminoguanidine hydrochloride (m. p. 161—162°; from ethanol). Dilution of the filtrate with ether (3 volumes) gave a white powder (filtrate F) (5·5—6·5 g., 49—58%), which consisted after crystallisation from ethanol–ether (1 : 3) of needles of the *hydrochloride*, m. p. 171—173° (decomp.) (Found: C, 31·8; H, 7·0; Cl, 15·1. $C_6H_{15}N_5S,HCl$ requires C, 31·9; H, 7·1; Cl, 15·7%). Filtrate F, on evaporation and dilution with ether, afforded more of the salt (8—12%).

Alternatively, the solution, after refluxing, was evaporated in a vacuum to remove most of the solvent, and the residual viscous liquid was dissolved in warm water (40 ml.) and treated with toluene-*p*-sulphonic acid monohydrate (10·5 g., 0·055 mole) in water (10 ml.). The white solid, collected at 0° and recrystallised from water (8 ml. per g., recovery 90%), consisted of needles (11·4 g., 60%) of the *toluene-p-sulphonate monohydrate*, m. p. 161—163° (decomp.) (Found: C, 41·9; H, 6·4; N, 18·85; S, 17·0. $C_6H_{15}N_5S,C_7H_8O_3S,H_2O$ requires C, 41·2; H, 6·6; N, 18·5; S, 16·9%). Boiling alkaline sodium plumbite slowly gave a small black precipitate and a strong smell of isocyanide.

The last-mentioned salt (0·38 g., 0·001 mole) dissolved on being stirred with water (5 ml.) and 3N-ammonia (0·5 ml., 0·0015 mole). Addition of 0·05M-picric acid (20 ml., 0·001 mole) gave the *picrate hydrate* (55%) as plates, m. p. 174—177° (decomp.) (from ethanol–light petroleum)

XUM

(Found: C, 33·4; H, 4·4; N, 25·0. $C_6H_{15}N_5S,C_6H_3N_3O_7,H_2O$ requires C, 33·0; H, 4·6; N, 25·7%).

(*c*) Interaction of aminoguanidine sulphate and butyl isothiocyanate in the presence of sodium (conditions and quantities as described for the methyl homologue, *c* above, except for time of refluxing, 2 hr.) gave, on acidification, crystals which were collected at 0° (5·7—6·5 g.). Recrystallisation from very little ethanol–light petroleum or preferably water (20 ml. per g., recovery 70—80%) gave needles (4·3—5·2 g., 50—60%) of *3-amino-4-butyl-5-mercapto-1,2,4-triazole*, m. p. 151—153° (Found: C, 41·9; H, 6·8. $C_6H_{12}N_4S$ requires C, 41·9; H, 7·0%). It had a wide unsymmetrical absorption maximum defined by λ 230, 240, 250, 260 mμ (log ε 4·30, 4·36, 4·35, 4·30), followed by a steep drop in absorption towards the longer wavelengths.

(*d*) A solution of the toluene-*p*-sulphonate monohydrate (1·9 g., 0·005 mole) in 100% orthophosphoric acid (10 ml.) was heated at 130° during 1 hr., and the cooled liquid diluted with water (40 ml.) (slight evolution of hydrogen sulphide), kept at 0° during 1 hr., filtered, and treated with 0·05M-aqueous pricric acid (100 ml., 0·005 mole). The precipitate (1·6 g., 80%) gave, on crystallisation from 90% ethanol (20 ml. per g.) and finally ethanol (100 ml. per g.), *2-amino-5-butylamino-1,3,4-thiadiazole picrate*, m. p. 218—221° (decomp.) (Found: C, 36·0; H, 3·6; N, 25·1. $C_6H_{12}N_4S,C_6H_3N_3O_7$ requires C, 35·9; H, 3·7; N, 24·4%). Interaction at 120° during 30 min. gave the same product in 55% yield.

(*e*) A solution of the same reactant (0·005 mole) in acetic anhydride (12 ml.) was refluxed during 20 min. Addition of the brown liquid to warm water (40 ml.) gave a white solid (0·72 g., 56%) which crystallised from ethanol (25 ml. per g.) as needles of the *diacetyl derivative*, m. p. 206—209°, of 2-amino-5-*n*-butylamino-1,3,4-thiadiazole (Found: C, 47·3; H, 6·2; N, 21·9. $C_{10}H_{16}N_4O_2S$ requires C, 46·9; H, 6·25; N, 21·9%).

The diacetyl derivative (0·51 g., 0·002 mole) dissolved on being boiled with 3N-hydrochloric acid (6 ml.). After 30 min. the solution was basified with 3N-ammonia and the crystals collected after storage at 0° (0·3 g.). Recrystallisation from ethanol–light petroleum (b. p. 40—60°) (1 : 2) gave *2-amino-5-n-butylamino-1,3,4-thiadiazole*, m. p. 147—149° (0·22 g., 64%) (Found: C, 41·7; H, 7·0; N, 32·55. $C_6H_{12}N_4S$ requires C, 41·9; H, 7·0; N, 32·6%). The picrate had m. p. and mixed m. p. with material obtained as in (*d*) 218—220° (decomp.).

*The* S-*Benzyl Derivative* (III; R = Ph, R′ = $CH_2Ph$).—A solution of 1-amidino-4-phenylthiosemicarbazide toluene-*p*-sulphonate solvate (6·41 g., 0·015 mole) in boiling ethanol (25 ml.) and water (10 ml.) was cooled to 40°, and benzyl chloride (1·9 g., 0·015 mole) was added. The stirred liquid was treated with 3N-sodium hydroxide (10 ml., 0·03 mole) during 10 min., and stirring at room temperature continued during 1·5 hr. Neutralisation to pH 6·5 with glacial acetic acid (5—6 ml.) converted the purple cloudy liquid into a colourless clear solution, which began to deposit crystals immediately. These (5·1 g., 72%) were collected after 3 hr. at 0°, rinsed with a little water and crystallised from 95% ethanol (15 ml. per g., recovery 80%) or ethanol (40 ml. per g.), affording plates of the *toluene-p-sulphonate*, m. p. 181—183°, of the *S*-benzyl derivative (Found: C, 56·1; H, 5·0; N, 14·9; S, 13·95. $C_{15}H_{17}N_5S,C_7H_8O_3S$ requires C, 56·05; H, 5·3; N, 14·9; S, 13·6%). The product dissolved readily in 3N-sodium hydroxide; on boiling, the resulting purple solution evolved toluene-α-thiol.

A suspension of this salt (0·94 g., 0·002 mole) in cold ethanol (10 ml.) was treated with 3N-sodium hydroxide (2 ml., 0·006 mole), added to water (50 ml.), and extracted with ether. On evaporation at room temperature, the washed dried extracts gave a white solid, which was covered with light petroleum and collected (0·54 g., 90%). Crystallisation from 1 : 3 ethanol–light petroleum (20 ml., b. p. 40—80°) gave needles of *1-amidino-S-benzyl-4-phenylisothiosemicarbazide*, m. p. 88—90° (sintering at 82°) (Found: C, 59·6; H, 5·5; N, 23·5; S, 10·8. $C_{15}H_{17}N_5S$ requires C, 60·2; H, 5·7; N, 23·4; S, 10·7%).

(*a*) The above salt (0·94 g., 0·002 mole) in 3N-sodium hydroxide (4 ml.) was refluxed during 20 min., diluted with water (20 ml.), and *just* acidified with 3N-acetic acid. The precipitate, collected after storage at 0°, was dibenzyl disulphide, m. p. 68—70° (0·17 g., 70%). The filtrate, treated with 0·05M-picric acid (50 ml., 0·0025 mole), gave an immediate precipitate (0·63 g., 78%) of 3-amino-5-anilino-1,2,4-triazole picrate, m. p. and mixed m. p.[1] 228—231° (decomp.) (from 90% ethanol) (Found: C, 41·6; H, 2·8. Calc. for $C_8H_9N_5,C_6H_3O_7N_3$: C, 41·6; H, 3·0%).

(*b*) The toluene-*p*-sulphonate (0·94 g., 0·002 mole) of the benzyl derivative in aniline (5 ml.) was refluxed during 1 hr., treated with water (20 ml.), and steam-distilled. The residual liquid

XUM

deposited crystals which were collected at 0° (0·345 g., 90%); they consisted of 3-amino-5-mercapto-4-phenyl-1,2,4-triazole, m. p. and mixed m. p. 264—266° (decomp.) (from ethanol) (Found: C, 49·9; H, 4·3; N, 28·9; S, 16·55. Calc. for $C_8H_8N_4S$: C, 50·0; H, 4·2; N, 29·2; S, 16·7%).

(*c*) The free benzyl derivative, freshly liberated and extracted with ether from the toluene-*p*-sulphonate (2·35 g., 0·005 mole), was treated with aniline (10 ml.), the ether distilled off, and the residual liquid refluxed during 30 min., and steam-distilled to remove the aniline. The residual oily (O) and aqueous (A) phase were separated by decantation. The oil (O), dissolved in ethanol (5 ml.) and treated with picric acid (1·15 g., 0·005 mole) in hot ethanol (8 ml.) gave yellow needles (0·82 g., 32%) of 3-amino-5-benzylthio-4-phenyl-1,2,4-triazole picrate, m. p. and mixed m. p. (see below) 222—228° (decomp.) (Found: C, 49·3; H, 3·3%). The aqueous phase (A), treated with 0·05M-picric acid (50 ml., 0·0025 mole) gave 3-amino-5-anilino-1,2,4-triazole picrate (0·70 g., 35%), m. p. and mixed m. p.[1] 228—232° (decomp.) (Found: C, 41·4; H, 2·8. Calc. for $C_8H_8N_5,C_6H_3N_3O_7$: C, 41·6; H, 3·0%).

3-*Amino*-5-*benzylthio*-4-*phenyl*-1,2,4-*triazole picrate*, obtained from the authentic components[3] in ethanol, formed yellow needles, m. p. 226—228° (decomp.) (from 75% ethanol) (Found: C, 48·85; H, 3·4; N, 19·8. $C_{15}H_{14}N_4S,C_6H_3N_3O_7$ requires C, 49·3; H, 3·3; N, 19·2%).

1-*Amidino*-S-*benzyl*-4-p-*tolylisothiosemicarbazide*.—The thiosemicarbazide toluene-*p*-sulphonate (3·95 g., 0·01 mole) dissolved, when to its stirred suspension in ethanol (20 ml.), water (10 ml.), and benzyl chloride (1·27 g., 0·01 mole) there was added 3N-sodium hydroxide (6·7 ml., 0·02 mole) dropwise during 10 min. at room temperature. Stirring was continued during 3 hr., the liquid acidified with 3N-acetic acid, and the solid collected after 24 hr. at 0°. Crystallisation from ethanol–ether (3 ml. each, per g.) and then from ethanol alone gave prisms (3·4 g., 70%) of the *toluene*-p-*sulphonate*, m. p. 145—147° (Found: C, 56·7; H, 5·7; N, 15·0. $C_{16}H_{19}N_5S,C_7H_8O_3S$ requires C, 56·9; H, 5·6; N, 14·4%), of the derivative.

This salt with sodium hydroxide or aniline gave, as above, 3-amino-5-*p*-toluidino-1,2,4-triazole picrate (60%), m. p. and mixed m. p. 235—238° (decomp.), or 3-amino-5-mercapto-4-*p*-tolyl-1,2,4-triazole, m. p. and mixed m. p. 278—280° (decomp.), respectively.

In the presence of an excess of toluene-*p*-sulphonic acid, the product was isolated as the *ditoluene*-p-*sulphonate*, m. p. 186—188° (white powder from ethanol), also formed from equimolar proportions of the monotoluene-*p*-sulphonate and toluene-*p*-sulphonic acid in 50% ethanol (Found: C, 54·4; H, 5·5; N, 10·7; S, 14·35. $C_{16}H_{19}N_5S,2C_7H_8O_3S$ requires C, 54·8; H, 5·3; N, 10·65; S, 14·6%).

3-*Amino*-5-p-*toluidino*-1,2,4-*triazole picrate*, obtained nearly quantitatively from the authentic components in ethanol, had m. p. 235—238° (decomp.) (from 90% ethanol) (Found: C, 42·9; H, 3·2. $C_9H_{11}N_5,C_6H_3N_3O_7$ requires C, 43·1; H, 3·35%). (Erratum: Part I, *J.*, 1960, 3437. On p. 3442, line 25: *For* 3-amino-5-anilino-1,2,4-triazole picrate, *read* 3-amino-5-*p*-toluidino-1,2,4-triazole picrate.)

*Semicarbazide Series*

1-*Amidino*-4-*phenylsemicarbazide*.—A suspension of aminoguanidine hydrochloride (2·21 g., 0·02 mole) in dimethylformamide (8 ml.) was treated with phenyl isocyanate (2·4 g., 0·02 mole) (slightly exothermic reaction). The mixture was kept at 100° during 15 min., and the resulting liquid stirred into water (75 ml.). The precipitate, collected and crystallised from ethanol, was *s*-diphenylurea (0·2 g.), m. p. and mixed m. p. 237—239°. Addition of toluene-*p*-sulphonic acid monohydrate (4·75 g., 0·025 mole) to the filtrate gave a precipitate (5·25—6·2 g., 72—85%), which was collected at 0°, rinsed with a little ice-water, and recrystallised from water and then from 1 : 2 ethanol–light petroleum (b. p. 40—80°), affording prisms of 1-*amidino*-4-*phenylsemicarbazide toluene*-p-*sulphonate*, m. p. 182—185° (decomp.) (Found: C, 48·75; H, 5·5; N, 19·1. $C_8H_{11}N_5O,C_7H_8O_3S$ requires C, 49·3; H, 5·2; N, 19·2%).

Interaction in anhydrous pyridine (10 ml.) at 100° during 1 hr. or at its b. p. during 30 min. gave the above product in 24 and 34% yield, respectively, the formation of carbanilide being correspondingly increased (0·8—1·6 g.).

The toluene-*p*-sulphonate (0·003 mole) dissolved instantly in 3N-sodium hydroxide (3 ml.) at room temperature, giving a red solution. Because of its very high solubility, the base was not isolated in the pure state.

The *picrate*, prepared from equimolar quantities of the toluene-*p*-sulphonate and picric acid

(0·0025 mole) in ethanol (10 ml.), formed needles, m. p. 236—239° (decomp.) (from 80% ethanol) (Found: C, 40·1; H, 3·35. $C_5H_{11}N_5O,C_6H_3N_3O_7$ requires C, 39·8; H, 3·3%.).

*Reactions of* 1-*Amidino*-4-*phenylsemicarbazide Toluene*-p-*sulphonate.*—(a) *With acetic anhydride.* A solution of the reactant (0·91 g., 0·0025 mole) in acetic anhydride (10 ml.) was kept at 120—125° during 20 min., then stirred into water (50 ml.); after the anhydride had dissolved, 0·05M-picric acid (50 ml., 0·0025 mole) was added. The resulting precipitate was crystallised from 90% ethanol (30 ml. per g.), giving needles of 1-N-*acetylamidino*-4-*phenylsemicarbazide picrate*, m. p. 194—198° (decomp., subject to the rate of heating) (0·70 g., 60%) (Found: C, 41·4, 41·3; H, 3·55, 3·4; N, 24·45. $C_{10}H_{13}N_5O_3,C_6H_3N_3O_7$ requires C, 41·4; H, 3·45; N, 24·1%).

This picrate (0·23 g., 0·0005 mole) in 3N-hydrochloric acid (8 ml.) was boiled during 15 min. The hot filtered liquid deposited yellow needles (0·12 g., 55%) of 1-amidino-4-phenylthiosemicarbazide picrate, m. p. and mixed m. p. 235—238° (decomp.) (from 80% ethanol) (Found: C, 39·9; H, 3·3%).

The *diacetyl derivative* of 3-amino-5-anilino-1,2,4-triazole, prepared by boiling the triazole (0·35 g., 0·002 mole) in acetic anhydride (3 ml.) during 15 min., formed needles (50%), m. p. 159—161° (from ethanol) (Found: C, 55·5; H, 5·05; N, 28·0. $C_{12}H_{13}N_5O_2$ requires C, 55·6; H, 5·0; N, 27·0%).

(b) *With concentrated sulphuric acid.* The reactant (1·825 g., 0·005 mole) dissolved readily in concentrated sulphuric acid (5 ml.) at room temperature. After 30 min. at 100° the pale brown liquid was added to ice (60 g.); the white powder which slowly separated was collected after 2 hr. at 0° (1·10 g., 80%). Two crystallisations from boiling water gave 1-*amidino*-4-p-*sulphophenylsemicarbazide*, m. p. 276—279° (decomp.) (Found: C, 35·1; H, 3·6; N, 25·8; S, 11·8. $C_8H_{11}N_5O_4S$ requires C, 35·2; H, 4·0; N, 25·6; S, 11·7%). This (2·73 g.) in 3N-sodium hydroxide (25 ml.) was refluxed during 2 hr. The crystalline deposit which separated on 12 hours' storage at 0° was collected and redissolved in boiling water (6 ml.) and the filtered liquid was acidified with 3N-hydrochloric acid (1 ml.), giving sulphanilic acid (0·45 g., 26%), decomp. above 300° (orange dye on diazotisation and coupling with β-naphthol) (Found: C, 41·7; H, 3·7; N, 8·0; S, 17·8. Calc. for $C_6H_7NO_3S$: C, 41·6; H, 4·05; N, 8·1; S, 18·5%); its ultraviolet absorption was identical with that of an authentic specimen.

(c) *With sodium hydroxide.* The toluene-*p*-sulphonate (0·005 mole) was recovered (60%) after being boiled in 3N-sodium hydroxide (10 ml.) (followed by acidification). When the salt was distilled with this reagent during 20 min., the distillate contained aniline (isolated as benzanilide, 65%).

1-*Amidino*-4-p-*tolylsemicarbazide.*—Interaction of aminoguanidine hydrochloride and *p*-tolyl isocyanate (0·02 mole) in dimethylformamide gave, by the above procedure, plates (5·46 g., 72%) of the *semicarbazide toluene*-p-*sulphonate*, m. p. 225—228° (decomp.) (Found: C, 50·8; H, 5·65. $C_9H_{13}N_5O,C_7H_8O_3S$ requires C, 50·7; H, 5·5%).

This salt (0·0025 mole) in 85% ethanol (15 ml.), treated with saturated ethanolic picric acid (0·0025 mole), deposited the *picrate* (80%) as needles, m. p. 236—239° (decomp.) (from 75% ethanol) (Found: C, 41·8; H, 3·7. $C_9H_{13}N_5O,C_6H_3N_3O_7$ requires C, 41·3; H, 3·7%).

1-*Amidino*-4-*butylsemicarbazide.*—Interaction of aminoguanidine hydrochloride and butyl isocyanate (0·02 mole each) in dimethylformamide (5 ml.) at 100° during 45 min., addition of the liquid to ice-water (20 ml.), and treatment of the clear solution with toluene-*p*-sulphonic acid monohydrate (4·75 g., 0·025 mole) gave crystals (5 g.) at 0° during 24 hr. Crystallisation from ethanol–ether (3 and 5 ml. per g.) gave the solvated *toluene*-p-*sulphonate*, m. p. 132—134° (decomp.) (4·35 g., 56%) (Found: C, 46·6; H, 7·3; N, 17·4. $C_6H_{15}N_5O,C_7H_8O_3S,C_2H_5{\cdot}OH$ requires C, 46·0; H, 7·4; N, 17·9%).

The *picrate* formed needles, m. p. 218—221° (decomp.) (from ethanol) (Found: C, 35·75; H, 4·5. $C_6H_{15}N_5O,C_6H_3N_3O_7$ requires C, 35·8; H, 4·5%).

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XUM

## 1018. *Manganese(II) Chloride Complexes. Part I. Stability Constants.*

By D. F. C. Morris and E. L. Short.

The existence of the complex species $MnCl^+$, $MnCl_2$, and $MnCl_3^-$ in aqueous solution has been established and their stability constants have been measured by a cation-exchange method. Manganese-54 has been employed as a tracer. The values obtained for the stability constants $\beta_j = [MnCl_j^{(2-j)+}]/[Mn^{2+}][Cl^-]^j$, valid for 20° and ionic strength 0·691M maintained with perchloric acid are: $\beta_1$, 3·85 ± 0·15; $\beta_2$, 1·80 ± 0·1; $\beta_3$, 0·44 ± 0·08.

Chloride complexes of manganese(II) in aqueous solution have been studied previously by anion-exchange,[1] spectrophotometric,[2] refractometric,[3] and conductance[4] methods. Most of this work has provided only qualitative information concerning the stability of the species.

In the present study $^{54}Mn$ has been used as tracer, together with a cation-exchange resin, to determine stability constants of manganese(II) chloride complexes. The resin, Zeo-Karb 225, has been employed in the $H^+$-form, and the ionic strength of the solutions has been kept constant (0·691M) by means of perchloric acid. The distribution of the radiomanganese at equilibrium between the ion-exchange resin and the complex solutions has been determined by $\gamma$-ray scintillation counting. The conditions employed were similar to those used by us in a study of zinc halide complexes,[5] and the results obtained should be comparable with those for the zinc systems.

The work forms part of a systematic investigation of halide species formed in solution by metals of the first transition series in oxidation state +2. Manganese-54 has a half-life of 291 days. It decays by electron capture with the emission of $\gamma$-rays of energy 0·84 Mev.

The method used to derive the individual stability constants, $\beta_j = [MnCl_j^{(2-j)+}]/[Mn^{2+}][Cl^-]^j$ ($j = 1, 2, \ldots n$), has been developed from that due to Fronaeus.[6] It is based on the assumption that no polynuclear manganese complexes are formed either in solution or in the resin phase, which is a reasonable presumption since the total metal concentration was very low ($7·6 \times 10^{-6}$M) and the solutions were of quite high acidity (0·691M). Moreover, in a study of the distribution of $Mn^{II}$ between hydrochloric acid and tri-n-butyl phosphate[7] no evidence of the existence of polynuclear complexes was observed with concentrations of manganese in the range $2·55 \times 10^{-6}$M to $1·024 \times 10^{-4}$M.

The following notation has been used (cf. Carleson and Irving[8]):

$C'_{Mn}, C'_{Cl}$ = total concentrations (moles/l.) of manganese and chloride in solutions before addition of the ion-exchange resin.

$C_{Mn}, C_{Cl}$ = corresponding total concentrations in the solution after equilibration with the resin.

$[M]$ = equilibrium concentration of a species in aqueous solution.

$[M]_R$ = equilibrium concentration of a species in the resin phase (moles/g. of dry resin).

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$a'$ = corrected activity (counts per min. per 2 ml.) of $^{54}Mn$ in solution before addition of the resin.

$a$ = corresponding activity of $^{54}Mn$ in the solution after equilibration with the ion-exchanger.

$\phi = (C_{Mn})_R/C_{Mn}$.

$X = 1 + \sum_{j=1}^{n} \beta_j[Cl^-]^j$; $X_j = (X_{j-1} - \beta_{j-1})/[Cl^-]$; $(X_0 = X;\ \beta_0 = 1)$.

$v$ = initial volume of the solution.

$v\delta$ = volume at equilibrium (where the factor $\delta$ is due to the swelling of the dry resin in contact with solution).

$m$ = weight of the dry resin used.

With this notation, it follows that at equilibrium:

$$C_{Mn} = [Mn^{2+}] + [MnCl^+] + [MnCl_2] + \ldots$$

$$= [Mn^{2+}](1 + \sum_{j=1}^{n} \beta_j[Cl^-]^j).$$

Also, if it is assumed that the concentration of complexes with zero or negative charges in the resin is negligible, then

$$(C_{Mn})_R = [Mn^{2+}]_R + [MnCl^+]_R \quad (1)$$

(Kraus, Michelson, and Nelson [9] have demonstrated strong sorption of some negatively charged chloro-complexes by cation-exchange resins, particularly from solutions of very high ionic strength. However, they have shown that this effect is essentially negligible in the case of $Mn^{II}$.)

Application of the law of mass action to the exchange equilibria

$$Mn^{2+} + 2(H^+)_R \rightleftharpoons 2H^+ + (Mn^{2+})_R$$

$$MnCl^+ + (H^+)_R \rightleftharpoons H^+ + (MnCl^+)_R$$

gives the expressions

$$[Mn^{2+}]_R/[Mn^{2+}] = k_0[H^+]_R^2/[H^+]^2 = l_0;\ [MnCl^+]_R/[MnCl^+] = k_1[H^+]_R/[H^+] = l_1 \quad (2)$$

Here $k_0$ and $k_1$ are functions of four activity coefficients. However, if the load $(C_{Mn})_R$ is kept reasonably constant and $\ll[H^+]_R$, both $[H^+]_R$ and the activity coefficients in the resin phase are effectively constant. These conditions were satisfied in the present work and, since $[H^+]$ was kept constant as was the ionic strength of the aqueous phase, $k_0$, $k_1$, and $l_0$, $l_1$ could be presumed to be constants. The distribution of manganese between resin and solutions is given by

$$\phi = (C_{Mn})_R/C_{Mn} = l_0(1 + l_1'[Cl^-])/X \quad (3)$$

from equation (2), the definition of $\beta_1$, and where $l_1' = l_1\beta_1/l_0$. Values for $\phi$ could be obtained from experimental results by means of the relation

$$\phi = v(a' - a\delta)/ma. \quad (4)$$

Since in the experiments $C_{Mn} \ll C_{Cl}$, $[Cl^-]$ was obtained with sufficient accuracy from the relationship $[Cl^-] \approx C_{Cl} = C_{Cl}'/\delta$. One could thus obtain corresponding values of $\phi$ and $[Cl^-]$ which must satisfy equation (3).

In order to determine the desired stability constants $\beta_j$, use was made of two new parameters, *viz.*:

$$\phi_1 = (l_0\phi^{-1} - 1)/[Cl^-], \quad (5)$$

$$f = (l_0\phi^{-1}\{(\beta_1 - l_1')[Cl^-] - 1\} + 1)/[Cl^-]^2. \quad (6)$$

[9] Kraus, Michelson, and Nelson, *J. Amer. Chem. Soc.*, 1959, **81**, 3204.

By substitution of the value of $\phi$ from equation (3) the following relationships are obtained:

$$\phi_1 = \frac{\beta_1 - l_1' + [Cl^-]X_2}{(1 + l_1'[Cl^-])} \quad (7)$$

$$f = \frac{\beta_1(\beta_1 - l_1') - \beta_2 + [Cl^-]\{X_2(\beta_1 - l_1') - X_3\}}{(1 + l_1'[Cl^-])} \quad (8)$$

Since $X_j = \sum_{i=j}^{n} \beta_i[Cl^-]^{i-j}$ is always a monotonic increasing function of $[Cl^-]$,

$$\phi_1^0 = \lim_{[Cl^-]\to 0} \phi_1 = \beta_1 - l_1', \quad (9)$$

$$f^0 = \lim_{[Cl^-]\to 0} f = \beta_1(\beta_1 - l_1') - \beta_2. \quad (10)$$

The necessary graphical extrapolations can be made as illustrated in Fig. 1. By combining equations (5), (6), and (7), it can be shown that

$$f = \beta_1\phi_1 - X_2. \quad (11)$$

Then, if $\Delta f = f - f^0$, and $\Delta\phi_1 = \phi_1 - \phi_1^0$,

$$\Delta f/[Cl^-] = (\beta_1\Delta\phi_1/[Cl^-]) - \beta_3 - \beta_4[Cl^-]. \quad (12)$$

In the present study a plot of $\Delta f/[Cl^-]$ against $\Delta\phi_1/[Cl^-]$ is a straight line (cf. Fig. 2) even with the higher values of $[Cl^-]$. It appears, therefore, that $\beta_4 \approx 0$ under the conditions of our experiments. The stability constant $\beta_1$ follows from the slope of the rectilinear plot, and $\beta_3$ may be evaluated from the intercept. The value of $\beta_2$ may be obtained from equation (10).

As our work has been performed at an appreciable acidity, there should be no complications due to hydrolysis of the hydrated $Mn^{2+}$ ion ($K_H \approx 2{\cdot}5 \times 10^{-11}$) or to the formation of hydroxy-halide complexes.

## Experimental

Manganese-54 of high specific activity was supplied as the chloride in aqueous solution by the Radiochemical Centre, Amersham. The tracer was converted into perchlorate by repeated evaporation with small quantities of perchloric acid, and a stock solution was made up. Afterwards tests for traces of chloride were carried out periodically and were always negative. Solutions of hydrochloric and perchloric acid used in the work were prepared from "AnalaR" materials.

The cation-exchange resin Zeo-Karb 225 (8% DVB; 30—50 mesh) was transformed into the $H^+$-form, dried over "Anhydrone," and stored in a closed bottle. The exchange capacity was found to be 3·64 milliequiv. per g. of "Anhydrone"-dried resin.

Distribution measurements were performed by mechanically shaking solutions (10 ml., $v$) of manganese complexes ($7{\cdot}6 \times 10^{-6}$M), made up from stock radiomanganese, hydrochloric acid, and perchloric acid, with portions (0·75 g., $m$) of dry resin in 50-ml. Pyrex tubes fitted with ground-glass stoppers. All experiments were performed at 20° ± 1°. Shaking was for at least 36 hr. to ensure attainment of equilibrium. After equilibration, 2 ml. of each aqueous phase were accurately pipetted into standard Polythene counting cups and counted at constant geometry with a NaI(Tl) $\gamma$-ray scintillation counter (type 1186A). The background count was subtracted from the measured counting rates to give the corrected activities, $a$. The corrected counting rate of a standard reference solution of known manganese concentration was also determined at frequent intervals, to yield values for $a'$. No adsorption of radiomanganese on the walls of vessels was detected.

The swelling factor, $\delta$, was determined by shaking $v = 10$ ml. of standard halogen acid with $m = 0{\cdot}75$ g. of resin and determining the change in hydrogen-ion concentration after equilibration. The value was always found to be 0·95.

## Results and Discussion

The experimental results for the effect of hydrochloric acid concentration on the cation-exchange distribution, and the functions used in evaluating stability and other constants, are given in Table 1. Application of the graphical procedures is illustrated in Figs. 1 and 2. In order to obtain satisfactorily consistent series of functions, it was necessary to carry out a certain amount of curve-fitting within the limits of counting

Table 1.

| $[Cl^-]$ (mole/l.) | $10^3\phi$ (l./g.) | $\phi_1$ $(mole/l.)^{-1}$ | $f$ $(mole/l.)^{-2}$ | $\Delta f/[Cl^-]$ $(mole/l.)^{-3}$ | $\Delta\phi_1/[Cl^-]$ $(mole/l.)^{-2}$ |
|---|---|---|---|---|---|
| 0 | 59·97 | (0·871) | (1·557) | — | — |
| 0·01815 | 59·02 | 0·8563 | 1·492 | −3·581 | −0·815 |
| 0·03629 | 58·18 | 0·8443 | 1·438 | −3·279 | −0·736 |
| 0·07281 | 56·57 | 0·8244 | 1·343 | −2·911 | −0·640 |
| 0·1080 | 55·14 | 0·8111 | 1·277 | −2·593 | −0·556 |
| 0·1455 | 53·74 | 0·7968 | 1·204 | −2·426 | −0·510 |
| 0·1815 | 52·48 | 0·7863 | 1·151 | −2·237 | −0·467 |
| 0·2164 | 51·32 | 0·7790 | 1·104 | −2·093 | −0·425 |
| 0·2540 | 50·15 | 0·7709 | 1·066 | −1·933 | −0·394 |
| 0·2912 | 49·05 | 0·7653 | 1·030 | −1·812 | −0·363 |
| 0·3621 | 47·05 | 0·7598 | 0·9694 | −1·626 | −0·308 |
| 0·4274 | 45·28 | 0·7590 | 0·9230 | −1·483 | −0·262 |
| 0·4837 | 43·92 | 0·7555 | 0·8967 | −1·365 | −0·239 |
| 0·5788 | 41·72 | 0·7558 | 0·8574 | −1·209 | −0·199 |
| 0·6411 | 40·41 | 0·7550 | 0·8386 | −1·121 | −0·181 |

$C'_{Mn} = 7{\cdot}6 \times 10^{-6}$M.

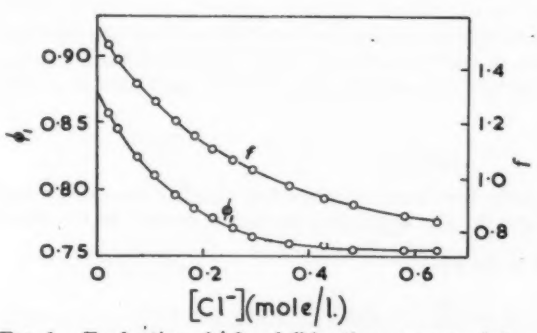


Fig. 1. Evaluation of $\phi_1^\circ$ and $f^\circ$ for the manganese(II) chloride system.

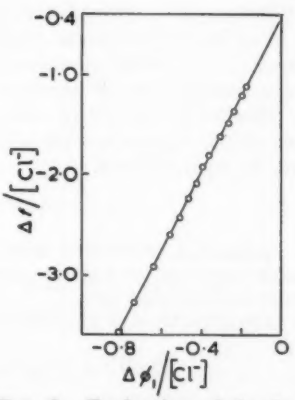


Fig. 2. Evaluation of $\beta_1$, $\beta_2$, and $\beta_3$ for the manganese(II) chloride system.

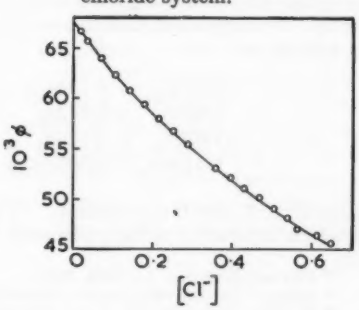


Fig. 3. Cation-exchange distribution of radio-manganese(II) with the resin Amberlite IR-120 ($H^+$).

errors (±0·5%). Final values obtained for the overall stability constants $\beta_j$ and the step constants $K_j = \beta_j/\beta_{j-1}$ are listed in Table 2.

TABLE 2.

Stability constants for manganese(II) chloride complexes, valid for 20° and 0·691M-perchloric acid.

| $\beta_1$ | $\beta_2$ | $\beta_3$ | $K_1$ | $K_2$ | $K_3$ |
|---|---|---|---|---|---|
| 3·85 ± 0·15 | 1·80 ± 0·1 | 0·44 ± 0·08 | 3·85 | 0·47 | 0·24 |

In addition to the experiments with Zeo-Karb 225, similar measurements were made with the cation-exchange resin Amberlite IR-120 in the $H^+$-form. Results for the effect of hydrochloric acid concentration on the distribution of radiomanganese with this other resin are plotted in Fig. 3. The curve shown in the diagram has been computed from equation (3), with the stability constants of Table 2, $l_0 = 67{\cdot}70 \times 10^{-3}$, and $l_1' = 2{\cdot}966 \times 10^{-3}$. It is apparent that the cation-exchange distribution variations with both Zeo-Karb 225 and Amberlite IR-120 are compatible with the stability constants derived in the present work. The uncertainties in the values for the stability constants given in Table 2 have been estimated from the results of several calculations of values for $\beta_j$ by the use of a relaxation method (see Appendix).

Our study provides no evidence for the existence of the ion $MnCl_4^{2-}$ in solution in the range $[Cl^-] \leqslant 0{\cdot}64$M, though crystalline compounds $[Ph_3MeAs]_2[MnCl_4]$ and $[Et_4N]_2[MnCl_4]$ have been prepared [10] which are uni-bivalent electrolytes in solvents such as nitromethane.

Studies of the solvent extraction of tracer manganese from aqueous chloride solutions and of the Raman spectra and structure of manganese(II) chloride complexes in solution will be reported later.

## APPENDIX

Relaxation methods [11] have recently been used in computing stability constants [12] from results obtained by various procedures.[13] The application of such a method to the present study is illustrated here.

Equation (3) may be rearranged in the form

$$\beta_1\phi[Cl^-] + \beta_2\phi[Cl^-]^2 + \beta_3\phi[Cl^-]^3 - \beta_1 l_1[Cl^-] - (l_0 - \phi) = 0.$$

Since values of $\phi$, $[Cl^-]$, and $l_0$ are known from experimental results, this is an equation containing four unknowns, $\beta_1$, $\beta_2$, $\beta_3$, and $(\beta_1 l_1)$. Hence, by taking four sets of corresponding values for $\phi$ and $[Cl^-]$ and using the extrapolated value for $l_0$ a set of simultaneous equations can be set up. For typical data obtained on using the resin Zeo-Karb 225, four such equations may be written as:

$$\begin{aligned}
10{\cdot}712\beta_1 &+ 0{\cdot}1944\beta_2 + 0{\cdot}00353\beta_3 - 181{\cdot}5\beta_1 l_1 - 9{\cdot}68 &= R,\\
5{\cdot}955\beta_1 &+ 0{\cdot}643\beta_2 + 0{\cdot}06946\beta_3 - 108\beta_1 l_1 - 4{\cdot}83 &= S,\\
17{\cdot}037\beta_1 &+ 6{\cdot}169\beta_2 + 2{\cdot}234\beta_3 - 362{\cdot}1\beta_1 l_1 - 12{\cdot}92 &= T,\\
2{\cdot}4148\beta_1 &+ 1{\cdot}3976\beta_2 + 0{\cdot}80894\beta_3 - 57{\cdot}88\beta_1 l_1 - 1{\cdot}825 &= U,
\end{aligned}$$

where $R$, $S$, $T$, and $U$ are residuals. A unit relaxation operations table may then be constructed in which the matrix of the coefficients is the transpose of the matrix of the original equation.

[10] Gill and Nyholm, *J.*, 1959, 3997.
[11] Shaw, "An Introduction to Relaxation Methods," Dover Publns., New York, 1953.
[12] Watkins and Jones, *J. Inorg. Nuclear Chem.*, 1961, **16**, 187.
[13] Leden, *Z. phys. Chem.*, 1941, *A*, **188**, 160; Bjerrum, "Metal Ammine Formation in Aqueous Solution," P. Haase, Copenhagen, 1957; Eriksson and Ringbom, *Acta Chem. Scand.*, 1953, **7**, 1105; Eriksson, *ibid.*, p. 1146; DeFord and Hume, *J. Amer. Chem. Soc.*, 1951, **73**, 5321; DeFord, Hume, and Cave, *ibid.*, p. 5323.

This Table shows the change in the residual brought about by a unit change in an unknown. For the present example the unit operations table results in:

| | $\Delta(R)$ | $\Delta(S)$ | $\Delta(T)$ | $\Delta(U)$ |
|---|---|---|---|---|
| $\Delta\beta_1$ | 10·712 | 5·955 | 17·04 | 2·415 |
| $\Delta\beta_2$ | 0·1944 | 0·643 | 6·17 | 1·398 |
| $\Delta\beta_3$ | 0·00353 | 0·0695 | 2·234 | 0·8089 |
| $\Delta(\beta_1 l_1)$ | −181·5 | −108 | −362·1 | −57·88 |

| | $R$ | $S$ | $T$ | $U$ |
|---|---|---|---|---|
| $\Delta\beta_j = \Delta(\beta_1 l_1) = 0$ | −9·68 | −4·83 | −12·92 | −1·825 |
| $\Delta(\beta_1 l_1) = 0·1$ | −27·83 | −15·56 | −49·13 | −7·613 |
| $\Delta\beta_1 = 3·0$ | 4·306 | 2·305 | 1·99 | −0·368 |
| $\Delta(\beta_1 l_1) = 0·1$ | −13·844 | −8·495 | −34·22 | −6·156 |
| $\Delta\beta_1 = 0·75$ | −5·81 | −4·0288 | −21·44 | −4·3448 |
| $\Delta\beta_2 = 1·5$ | −5·5184 | −3·0643 | −12·185 | −2·2478 |
| $\Delta\beta_2 = 0·44$ | −5·5168 | −3·0337 | −11·202 | −1·8919 |
| $\Delta\beta_2 = 0·3$ | −5·4585 | −2·8408 | −9·351 | −1·4005 |
| $\Delta\beta_1 = 0·1$ | −4·3873 | −2·2453 | −7·647 | −1·159 |
| $\Delta(\beta_1 l_1) = -0·021$ | −0·5758 | 0·02273 | −0·0429 | −0·01545 |
| $\Delta\beta_3 = 0·0191$ | −0·5757 | 0·024057 | −0·0002 | 0·0000 |

The relaxation table is then constructed; one way is annexed. After the residuals have been reduced suitably, the values for the stability constants and the other unknown constant ($\beta_1 l_1$) are obtained by summing the changes which have been made in each of the variables. In the present example: $\beta_1 = \sum\Delta\beta_1 = 3·85$, $\beta_2 = \sum\Delta\beta_2 = 1·8$, $\beta_3 = \sum\Delta\beta_3 = 0·459$, and $(\beta_1 l_1) = \Sigma\Delta(\beta_1 l_1) = 0·179$.

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## 1019. *Synthesis of* 3-O-p-*Coumaroylquinic Acid.*

By E. Haslam, R. D. Haworth, and G. K. Makinson.

A substance previously isolated from cider apples is shown by synthesis to be 3-*O*-*p*-coumaroylquinic acid. Its biogenetic relationship to chlorogenic acid is briefly discussed.

Chlorogenic acid was first isolated from coffee beans by Gorter [1] who showed it to be a derivative of quinic acid (Ia). Freundenberg [2] showed that the enzyme tannase hydrolysed chlorogenic acid to equimolar amounts of quinic and caffeic acid, and its structure as the 3-caffeic ester (Ib) of quinic acid was later deduced by Fischer and Dangschat [3] from its methylation and subsequent hydrolysis to 3,4-di-*O*-methylcaffeic acid and 1,4,5-tri-*O*-methylquinic acid (isolated as the 1,3-lactone). A synthesis of chlorogenic acid by Panizzi, Scarpati, and Oriente [4] has recently confirmed this structure. Since its initial isolation from coffee beans, chlorogenic acid has been found in other plant species [5] and the advent of modern methods of plant analysis, notably paper chromatography, has shown its widespread distribution in the fruit, leaves, and other tissues of a variety of dicotyledenous plants.[6] Paper-chromatographic analysis of the chemical constituents of plant tissues has also enabled additional related phenolic compounds to be identified and later isolated. Thus in 1958 Williams [7] isolated from cider apples a compound which

[1] Gorter, *Annalen*, 1907, **358**, 328.
[2] Freudenberg, *Ber.*, 1920, **53**, 232.
[3] Fischer and Dangschat, *Ber.*, 1932, **65**, 1037.
[4] Panizzi, Scarpati, and Oriente, *Experientia*, 1955, **11**, 383.
[5] Paech and Tracey, "Moderne Methoden der Pflanzenanalyse," Springer-Verlag, Berlin, 1955, Vol. III, p. 427.
[6] Bate-Smith, *Chem. and Ind.*, 1954, 1457; Hermann, *Pharmazie*, 1956, **11**, 433.
[7] Williams, *Chem. and Ind.*, 1958, 1200.

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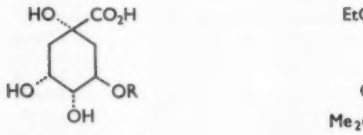
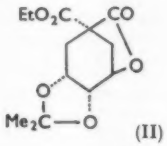
was shown to be a *p*-coumaric ester of quinic acid and Schütte, Langenbeck, and Böhme [8] described the isolation of a similar but not identical substance from *Antirrhinum majus*. Since the amount isolated did not allow a complete structural proof by chemical degradation, Williams,[7] on the basis of its paper-chromatographic similarity and probable biogenetic relation to chlorogenic acid, tentatively assigned to the compound from cider apples the structure of 3-*O*-*p*-coumaroylquinic acid (Ic). Paper chromatography has been used to show that this substance occurs also in tea, cacao, and quebracho leaves, and in apples and pears,[9] and its presence in other plant species, *e.g.*, *Crataegus*, *Betulaceae*, *Vaccinia*, has been established by similar techniques during this present work.



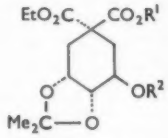
(Ia : R = H)

(Ib : R = ·CO·CH:CH·C$_6$H$_4$·OH)

(Ic : R = ·CO·CH:CH·C$_6$H$_4$·OH-*p*)



(II)



(IIIa : R$^1$ = R$^2$ = H)

(IIIb : R$^1$ = Me ; R$^2$ = H)

(IIIc : R$^1$ = CHPh$_2$ ; R$^2$ = H)

(IIId : R$^1$ = CHPh$_2$ ; R$^2$ = CO·CH:CH·C$_6$H$_4$·O·CO·OEt-*p*)

(IIIe : R$^1$ = CHPh$_2$ ; R$^2$ = CO·CH:CH·C$_6$H$_4$·OH-*p*)

Panizzi *et al.*[4] synthesised chlorogenic acid by esterification of the unsubstituted 3 position in the ester (IIIb) with 3,4-oxomethylenedioxycinnamoyl chloride, followed by removal of the isopropylidene group in acid and hydrolysis of the cyclic carbonate, ethoxycarbonyl, and methyl ester groups with barium hydroxide. In modifying this synthesis for the preparation of 3-*O*-*p*-coumaroylquinic acid it was sought in particular to protect the carboxyl group of quinic acid in such a way that it would be regenerated by acid; the diphenylmethyl group was chosen for this purpose.

The calculated amount of barium hydroxide converted the lactone (II) into 1-*O*-ethoxycarbonyl-4,5-*O*-isopropylidenequinic acid (IIIa) and this on treatment with diphenyldiazomethane [10] gave the diphenylmethyl ester (IIIc). Acylation of the unsubstituted 3-hydroxyl group with 4-*O*-ethoxycarbonylcinnamoyl chloride gave the ester (IIId), but removal of the protecting groups from this compound to give 3-*O*-*p*-coumaroylquinic acid was not achieved as planned. Treatment with aqueous acetic acid, in order to remove the acid labile isopropylidene and diphenylmethyl groups, gave an intractable gum which on the subsequent action of barium hydroxide gave small yields (2%) of the required 3-*O*-*p*-coumaroylquinic acid and appreciable quantities of *p*-coumaric acid, the former being isolated by counter-current distribution between ethyl acetate and water. In an attempt to reduce the amount of *p*-coumaric acid formed the ester (IIId) was treated with exactly two equivalents of sodium hydroxide, but under these conditions the 1-*O*-ethoxycarbonyl group was unusually stable and selective hydrolysis occurred with the formation of the ester (IIIe). This compound had a chromophore and fluorescence in ultraviolet light typical of esters of *p*-coumaric acid, and with diazomethane it gave a monomethyl ether. However, acid removed the isopropylidene, diphenylmethyl, and 1-*O*-ethoxycarbonyl groups, and 3-*O*-*p*-coumaroylquinic acid (Ic) was isolated. The product was identical with the natural sample (kindly supplied by Dr. A. H. Williams),

[8] Schütte, Langenbeck, and Böhme, *Naturwiss.*, 1957, **44**, 63.
[9] Cartwright, Flood, Roberts, and Williams, *Chem. and Ind.*, 1955, 1062; White and King, *Proc. Chem. Soc.*, 1957, 341; Griffiths, *Biochem. J.*, 1958, **70**, 120.
[10] Staudinger, Anthes, and Pfenninger, *Ber.*, 1916, **49**, 1932.

thus proving the tentative structure suggested in 1958. Hydrogenation of 3-*O*-*p*-coumaroylquinic acid gave the corresponding 3-*O*-*p*-hydroxyphenylpropionylquinic acid.

The biogenetic relation of 3-*O*-*p*-coumarylquinic acid to chlorogenic acid is fairly evident,[7] and the identification in potato tuber [11] of these two substances and a suggested 3-cinnamoyl derivative of quinic acid indicated that the last substance might give rise to the *p*-coumaroyl and caffeoyl derivatives by successive hydroxylation of the aromatic nucleus. Neisch [12] has similarly proposed the existence of a $C_6$—$C_3$ pool in which lignin precursors are derived from cinnamic acid by similar processes. Accordingly we attempted to convert 3-*O*-*p*-coumaroylquinic acid into chlorogenic acid by the action of the enzyme tyrosinase,[13] which it is believed can in certain cases convert monohydric into *o*-dihydric phenols, but so far we have been unable to bring about this transformation. Further experiments towards the elucidation of this relationship are in progress.

## Experimental

1-O-*Ethoxycarbonyl*-4,5-O-*isopropylidenequinic Acid* (IIIa) [with D. A. Lawton].—Considerable difficulty was experienced in the preparation of this compound as described [4] and the following method was used. 1-*O*-Ethoxycarbonyl-4,5-*O*-isopropylidenequinide [4] (II) (5·7 g.) was heated in ethanol (50 c.c.) containing acetone (15 c.c.) at 50° in an atmosphere of nitrogen. 0·23N-Barium hydroxide (85 c.c.) was added dropwise and then the mixture was heated at 60° for ½ hr., cooled to 5°, and treated with 2N-sulphuric acid until neutral. Removal of the barium sulphate, extraction of the aqueous solution with ethyl acetate (5 × 50 c.c.), and evaporation gave 1-*O*-ethoxycarbonyl-4,5-*O*-isopropylidenequinic acid which crystallised from ethyl acetate–light petroleum (b. p. 60—80°) as plates (4·5 g.), m. p. 150—152° (Panizzi *et al.*[4] give this m. p.), $\nu_{max.}$ 1747 cm.$^{-1}$ (KBr disc).

*Diphenylmethyl* 1-O-*Ethoxycarbonyl*-4,5-O-*isopropylidenequinate* (IIIc) [with D. A. Lawton].—A solution of diphenyldiazomethane [10] (4·8 g.) in chloroform (20 c.c.) was added to one of 1-*O*-ethoxycarbonyl-4,5-*O*-isopropylidenequinic acid (IIIa) (5·0 g.) in chloroform (100 c.c.), and the mixture refluxed for 6 hr. Removal of the solvent and crystallisation of the residue from ethyl acetate gave needles (6·7 g.) of *diphenylmethyl* 1-O-*ethoxycarbonyl*-4,5-O-*isopropylidenequinate*, m. p. 163° (Found: C, 66·1; H, 6·4. $C_{26}H_{30}O_8$ requires C, 66·4; H, 6·4%), $\nu_{max.}$ 1751 cm.$^{-1}$ (KBr disc).

4-O-*Ethoxycarbonylcinnamoyl Chloride*.—*p*-Coumaric acid was prepared by slight modifications of Wittmer and Raiford's method.[14] 4-*O*-Ethoxycarbonylcinnamic acid (1·8 g.), prepared from *p*-coumaric acid by Bonn's method,[15] was dissolved in dry benzene (25 c.c.) containing phosphorus pentachloride (1·6 g.) and refluxed for 1 hr. Removal of the solvent and crystallisation of the residue from light petroleum (b. p. 60—80°) gave needles (1·6 g.), m. p. 73—74°. 4-O-*Ethoxycarbonylcinnamoyl chloride* was characterised as its α-*naphthyl ester* (prepared in pyridine), m. p. 89—90° (Found: C, 72·4; H, 5·1. $C_{22}H_{18}O_5$ requires C, 72·9; H, 5·0%).

*Diphenylmethyl* 1-O-*Ethoxycarbonyl*-3-(4-O-*ethoxycarbonylcinnamoyl*)-4,5-O-*isopropylidenequinate* (IIId).—To the ester (IIIc) (1·18 g.) in benzene (25 c.c.) was added 4-*O*-ethoxycinnamoyl chloride and pyridine (2·5 c.c.). The mixture was refluxed for 3 hr. and left for 15 hr. at room temperature, after which it was washed with cold 2N-hydrochloric acid, saturated aqueous sodium hydrogen carbonate, and water, and dried ($MgSO_4$). Removal of the benzene gave a gum which crystallised from benzene–light petroleum to give the *product* (IIId) as prisms (2·4 g.), m. p. 108—109° (Found: C, 66·2; H, 5·8. $C_{38}H_{39}O_{12}$ requires C, 66·3; H, 5·8%), $\nu_{max.}$ (KBr disc) 1726 and 1756 cm.$^{-1}$.

*Diphenylmethyl* 1-O-*Ethoxycarbonyl*-3-p-*coumaroyl*-4,5-O-*isopropylidenequinate* (IIIe).—N-Sodium hydroxide (1·5 c.c.) was added dropwise with stirring to a solution of the ester (IIId) (1·0 g.) in methanol (25 c.c.). The solution was kept at 30° for ½ hr. and just acidified with N-hydrochloric acid. Water (25 c.c.) was added and the solution extracted with ethyl acetate (75 c.c.), to yield, on removal of the solvent and crystallisation from ethanol, needles (0·5 g.)

[11] Sondheimer, *J. Biol. Chem.*, 1960, **235**, 2418.
[12] Neisch, *Canad. J. Biochem. Physiol.*, 1959, 537.
[13] Mallette, Lewis, Ames, Nelson, and Dawson, *Arch. Biochem.*, 1948, **16**, 288.
[14] Wittmer and Raiford, *J. Org. Chem.*, 1945, **10**, 527.
[15] Bonn, *Ber.*, 1913, **46**, 4052.

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of the *product* (IIIe), m. p. 204—205° (Found: C, 68·0; H, 5·8; OEt, 7·0. $C_{25}H_{26}O_{10}$ requires C, 68·2; H, 5·9; OEt, 7·3%). The compound showed a bright blue fluorescence when exposed to ultraviolet light in the presence of ammonia vapour, and its infrared spectrum (KBr disc) showed absorption at 1717 and 1756 cm.$^{-1}$.

*Diphenylmethyl* 1-O-*Ethoxycarbonyl*-3-(4-O-*methyl*-p-*coumaroyl*)-4,5-O-*isopropylidene-quinate*.—A solution of diazomethane (0·42 g.) in ether (20 c.c.) was added to a suspension of the ester (IIIe) (0·35 g.) in benzene (100 c.c.) and the mixture left at 20° for 16 hr. Removal of the solvents and recrystallisation of the residue from ethanol gave the *methyl ether* as plates (0·25 g.), m. p. 212° (Found: C, 68·2; H, 6·0; OMe, 4·3. $C_{36}H_{38}O_{10}$ requires C, 68·6; H, 6·0; OMe, 4·9%), that do not fluoresce in ammonia vapour under ultraviolet light.

3-O-p-*Coumaroylquinic Acid* (Ic).—The ester (IIIe) (2·5 g.) was refluxed in 80% aqueous acetic acid (25 c.c.) for 6 hr. The solvent was removed at 30°, and the residue dissolved in saturated sodium hydrogen carbonate solution (40 c.c.) and extracted with ethyl acetate (50 c.c.). Acidification of the aqueous layer with 2N-sulphuric acid gave 3-O-p-*coumaroylquinic acid* which after two recrystallisations from water formed needles (0·5 g.), m. p. and mixed m. p. (with the natural product) 247—248° (Found: C, 56·5; H, 5·3. $C_{16}H_{18}O_8$ requires C, 56·8; H, 5·3%), had $[\alpha]_D^{20}$ −53·6° (*c* 1·04 in MeOH) (Williams gives $[\alpha]_D$ −53·5°). The ultraviolet ($\lambda_{max.}$ 250 mμ, ε 1·4 × $10^4$ in 95% EtOH) and infrared spectra (KBr disc, 1600, 1630, and 1710 cm.$^{-1}$) were identical with those of the natural product.

3-O-p-*Hydroxyphenylpropionylquinic Acid*.—3-*O*-*p*-Coumaroylquinic acid (0·13 g.) in ethanol (20 c.c.) was hydrogenated at 25°/1 atm. in the presence of 10% palladium–charcoal (0·1 g.) for 16 hr. Removal of the catalyst and solvent and crystallisation of the product from water gave the *propionyl derivative* as needles (0·1 g.), m. p. 201° (Found: C, 56·2; H, 6·0. $C_{16}H_{20}O_8$ requires C, 56·5; H, 5·9%), $[\alpha]_D^{20}$ −44·0° (*c* 0·32 in EtOH), $\nu_{max.}$ 1610 and 1725 cm.$^{-1}$.

We thank Dr. A. H. Williams (Long Ashton Research Station) for a sample of 3-*O*-*p*-coumaroylquinic acid isolated from cider apples, and Imperial Chemical Industries Limited for a grant and leave of absence to G. K. M. and for grants in aid of the work described.

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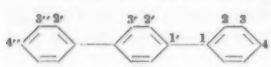
## 1020. *Isomer Ratios for the Mononitration of* p-*Terphenyl in Acetic Acid and Acetic Anhydride.*

By G. W. Gray and D. Lewis.

Quantitative data have been obtained for the ratios of the mononitro-isomers (4-, 2-, and 2′-) formed on nitration of *p*-terphenyl in glacial acetic acid at 20° and in acetic anhydride at 0°, 20°, 40°, and 80°. The results and their accuracy are discussed in general terms, and attention is drawn to the greater degree of *ortho*-substitution, *i.e.*, at the 2- and 2′-positions, which occurs in acetic anhydride. Isomer ratios published for the mononitration of biphenyl are reviewed and compared with the present results for *p*-terphenyl

France, Heilbron, and Hey [1] reported that the nitration of *p*-terphenyl in acetic acid with fuming nitric acid at 100° gave a 43% yield of 4,4″-dinitro-*p*-terphenyl, and that nitration in acetic anhydride at 45—50° gave the same product in 68% yield. These authors also obtained a 100% yield of 4,2′,4″-trinitro-*p*-terphenyl by nitrating the hydrocarbon in fuming nitric acid alone. Recently,[2] attempts to reproduce these and other nitrations reported by France, Heilbron, and Hey proved unsuccessful, and qualitative studies showed that there was considerably less nitration at the *para*-positions of *p*-terphenyl than France, Heilbron, and Hey found in their experiments. In fact, a close similarity was indicated between the *ortho* : *para*-isomer ratios for *p*-terphenyl and biphenyl. Quantitative data for the proportions of the isomers formed



(I)

[1] France, Heilbron, and Hey, *J.*, 1938, 1364.
[2] Culling, Gray, and Lewis, *J.*, 1960, 1547.

on mononitration of the hydrocarbon (I) are now presented (Table 1) in support of these recent findings.

TABLE 1.

| Expt. | Nitrating conditions [a] | | Proportions of isomers [b] (%) 2 | 2′ | 4 |
|---|---|---|---|---|---|
| N 5 | HOAc at 20° | | 25 | 12 | 63 |
| N 12 | ,, ,, | | — | — | 62 |
| N 14 | ,, ,, | | 25 | 12 | 63 |
| | | Mean | 25 | 12 | 62·7 |
| N 2 | $Ac_2O$ at 0° | | 40 | 20 | 40 |
| N 3 | ,, ,, | | 42 | 18 | 40 |
| | | Mean | 41 | 19 | 40 |
| N 10 | $Ac_2O$ at 20° | | 29 | 17 | 54 |
| N 13 | ,, ,, | | 32 | 17 | 51 |
| N 15 | ,, ,, | | 32 | 17 | 51 |
| | | Mean | 31 | 17 | 52 |
| N 18 | $Ac_2O$ at 40° | | — | — | 58 |
| N 24 | ,, ,, | | — | — | 52 |
| N 29 | ,, ,, | | 29 | 17 | 55 |
| N 30 | ,, ,, | | 29 | 18 | 53 |
| | | Mean | 29 | 17·5 | 54·5 |
| N 28 | $Ac_2O$ at 80° | | 31 | 14 | 55 |

[a] For details of the nitrating conditions, see Experimental section. [b] It is shown in the Experimental section under " accuracy of results," that the amount of 3-nitro-*p*-terphenyl is too small for detection. [c] Because of the limited accuracy of these determinations involving three component mixtures, we judge that not more than two significant figures are justified in quoting the individual results.

Table 2 makes possible a comparison between the observed positional order of reactivities for *p*-terphenyl and various theoretically predicted values, allowance being made for the number of positions of each type.

TABLE 2.

| | Positional order of reactivity |
|---|---|
| Found in all cases | $4 > 2 > 2' (\geqslant 3)$ |
| Reactivity number [a] | $4 = 2 > 2' \geqslant 3$ |
| Resonance theory | $4 = 2 > 2' >$ or $\geqslant 3$ |
| Free valence [b] | $2 > 2' > 4 > 3$ |

[a] Dewar, *J. Amer. Chem. Soc.*, 1952, **74**, 3341 *et seq.* [b] Buu-Hoï, Coulson, Daudel, Daudel, Martin, Pullman, and Pullman, *Rev. Sci.*, 1947, **85**, 1041.

No treatment predicts that the 4-position should be more reactive than the 2- or 2′-positions, and it is probable that this discrepancy arises from steric factors which prevent the *ortho*-positions from being attacked as easily as the exposed *para*-positions. The difference (0·05) between the reactivity numbers for the equally sterically affected 2- and 2′-positions corresponds to a two-fold difference in the rates of nitration at these positions (cf. 0·38 unit of reactivity number in phenanthrene corresponds to a seven-fold change in the rate of nitration [3]). On this basis, no substitution would be expected, and none was found, at the 3-position of *p*-terphenyl.

Turning to a consideration of the results themselves, the main feature is the increase in the ratio of *ortho*(2- + 2′)- to *para*(4)-substitution obtained on changing the solvent from acetic acid to acetic anhydride. The 63% yield of 4-nitro-*p*-terphenyl obtained by nitration in acetic acid at 20° is in good agreement with the preparative yield [2] of 52—54% for nitration in this solvent at 111°. If equation 39 of Augood and Williams [4] is used, a 63% yield of the 4-isomer will fall to 52% at 111°. If this equation 39 and the results for nitration in acetic anhydride at 0° are used, the calculated *ortho*(2- + 2′)- to *para*-ratio

[3] Dewar and Warford, *J.*, 1956, 3570.
[4] Augood and Williams, *Chem. Rev.*, 1957, 123.

should be 63 : 37 at 40°. In fact the results show a large decrease to a ratio of 48 : 52 at 20°, and to one of 46·5 : 54·5 at 40°. These changes cannot therefore be caused by the temperature differences, and nitrations at 80° were attempted to obtain more results. Unfortunately the products obtained were brown, indicating that the nitration products were undergoing further reaction at this high temperature. The single result obtained does, however, suggest that the ratio (45 : 55) is virtually the same as that at 40°.

Whilst it is reasonably well established that aromatic nitrations by solutions of nitric acid in acetic acid proceed by a mechanism involving the nitronium ion, there remains uncertainty in the case of nitrations in acetic anhydride. Paul [5] found that the nitration of benzene by nitric acid in acetic anhydride at 25° was approximately of the second order with respect to the nitric acid. The fact that the reaction is strongly suppressed by added nitrate ion led Paul to reject the idea that nitration was occurring by means of the ion pair $NO_2^+NO_3^-$ or molecular $N_2O_5$, and to favour instead attack by the nitronium ion:

$$HNO_3 + H^+ \rightleftharpoons H_2NO_3^+ \quad \text{(i)}$$

$$H_2NO_3^+ + Ac_2O \rightleftharpoons NO_2^+ + 2AcOH \quad \text{(ii)}$$

$$NO_2^+ + C_6H_6 \longrightarrow \left(C_6H_5\begin{smallmatrix}H\\NO_2\end{smallmatrix}\right)^+ \quad \text{(iii)}$$

Nitration at oxygen centres by nitric acid in acetic acid containing a small amount of acetic anhydride is also of second order with respect to the nitric acid.[6] Bonner interprets this in terms of nitration by $N_2O_5$, and more recently Norman and Radda [7] have explained the high *ortho* : *para*-ratio obtained on nitration of methyl phenethyl ether by acetyl nitrate in terms of displacement of nitrate ion from covalent dinitrogen pentoxide by the oxygen of the ether, forming an intermediate, $Ph{\cdot}CH_2{\cdot}CH_2{\cdot}O^+(Me){\cdot}NO_2$, which rearranges to the usual transition state for *ortho*-substitution. This apparently conflicting evidence for the nature of the attacking species in nitrations in acetic anhydride could be reconciled if in fact nitration in acetic anhydride proceeds by different mechanisms under different conditions. Indeed, the change in the isomer ratios for nitration of *p*-terphenyl in acetic anhydride at 0° and 20° was at first thought to support this idea.

However, semi-quantitative data (see Experimental section) show that the nitration of *p*-terphenyl is strongly retarded by added nitrate ion for both acetic acid and acetic anhydride media at 0° and 20°. Corresponding experiments conducted with added perchlorate ion showed that there was no retardation of the nitration, and the conclusion must be reached that the nitronium ion is the attacking species in all these experiments.

A comparison of the isomer ratios for nitration of *p*-terphenyl and biphenyl shows features of considerable interest (Table 3).

The results, for both *p*-terphenyl and biphenyl, fall into two distinct groups, although there is a considerable variation of the ratios within each set. Thus, in an acetic anhydride medium, a high *ortho* : *para*-ratio is obtained, whilst various other media result in a low *ortho* : *para*-ratio. de la Mare and Hassen [8,9] have commented that the isomer ratio obtained on nitration of biphenyl is dependent on the conditions of reaction, and indeed, the available data for the nitration of this hydrocarbon support the present results for *p*-terphenyl and demonstrate that a change from a high to a low *ortho* : *para*-ratio occurs on changing the nitrating medium from acetic anhydride to acetic acid.

It is, of course, well established [10] that higher proportions of *ortho*-substitution occur

[5] Paul, *J. Amer. Chem. Soc.*, 1958, **80**, 5329.
[6] Bonner, *J.*, 1959, 3908.
[7] Norman and Radda, *Proc. Chem. Soc.*, 1960, 423.
[8] de la Mare and Hassen, *J.*, 1957, 3004.
[9] de la Mare and Hassen, *J.*, 1958, 1519.
[10] Griffiths, Walkey, and Walker, *J.*, 1934, 631; Halvarson and Melander, *Arkiv Kemi*, 1957, **11**, 77; Holleman, *Chem. Rev.*, 1925, **1**, 187; Arnall and Lewis, *J. Soc. Chem. Ind.*, 1929, **48**, 159T.

TABLE 3.

| Nitrating conditions | | | | | Ratio (%) * *ortho-* | Ratio (%) * *para-* |
|---|---|---|---|---|---|---|
| Biphenyl, $Ac_2O$–$HNO_3$ (*d* 1·38) at 53° (87%) | | | | [a] | 58 | 42 |
| ,, | ,, | (*d* 1·5) | 0° | [b] | 68 | 32 |
| ,, | ,, | ,, | ,, | [c] | 67 | 33 |
| ,, | ,, | ,, | ,, | [d] | 77 | 23 |
| *p*-Terphenyl, | ,, | ,, | ,, | | 60 | 40 |
| Biphenyl, HOAc–$HNO_3$ (*d* 1·5) at 70—90° (*ca.* 77%) | | | | [e] | 36 | 64 |
| ,, | $H_2SO_4$–$HNO_3$ (*d* 1·5)–$H_2O$ at 35—40° (91%) | | | [f] | 37 | 63 |
| ,, | $HNO_3$ (*d* 1·448) at *ca.* 50° | | | [g] | 53 | 47 |
| ,, | liquid $N_2O_4$ at room temp. | | | [h] | 35 | 65 |
| *p*-Terphenyl, HOAc–$HNO_3$ (*d* 1·5) at 20° | | | | | 37 | 63 |

* In these cases for which the isomer ratios have been normalised to 100%, the actual yields recovered are given in parentheses.

[a] Hayashi, Inana, and Ishikawa, *J. Pharm. Soc. Japan*, 1959, **79**, 972. [b] Simamura and Mizuno, *Bull. Chem. Soc. Japan*, 1957, **30**, 196. [c] Warford, Ph.D. Thesis, London University, 1956. [d] Dewar, Mole, Urch, and Warford, *J.*, 1956, 3572. [e] Bell, Kenyon, and Robinson, *J.*, 1926, 1239. Jenkins, McCullough, and Booth, *Ind. Eng. Chem.*, 1930, **22**, 31. [f] Gull and Turner, *J.*, 1929, 491. [g] Shorygin, Topchiev, and Ananina, *J. Gen. Chem.* (*U.S.S.R.*), 1938, **8**, 981.

when acetanilide and anisole are nitrated with acetyl nitrate than with nitric acid or mixed acid, and Paul [11] considers that the *ortho* : *para*-ratios for certain substitutions can be changed by the influence of the dielectric constant of the medium on the polar character of a substituent in the aromatic substrate. Since, however, biphenyl and *p*-terphenyl are both non-polar, Paul's hypothesis can hardly be applied to the substitution of these hydrocarbons, and the change in the isomer ratios when the solvent is changed.

The high *ortho* : *para*-ratios which have been obtained by other workers [7,11] for certain nitrations in acetic anhydride have, therefore, been explained by the influence of the dielectric properties of the medium on the polarity of a ring-substituent bond, or by the attack of dinitrogen pentoxide at an oxygen centre in a side chain attached to the aromatic ring. Neither explanation can be applied to the high *ortho* : *para*-ratios for nitrations of biphenyl and *p*-terphenyl in acetic anhydride and, further, it is clear that this high ratio for *p*-terphenyl is obtained under conditions which involve the nitronium ion, not dinitrogen pentoxide, as the electrophilic reagent. The rapid decrease in the *ortho* : *para*-ratio for the nitration of *p*-terphenyl in acetic anhydride to approximately 1 : 1 when the temperature is raised from 0° to 20° is also of considerable interest, but further work is necessary before an explanation of these effects can be proposed.

## EXPERIMENTAL

*Materials and Media.*—Fuming nitric acid (*d* 1·504), acetic anhydride, and acetic acid ("AnalaR") were commercial products used without further purification. *p*-Terphenyl (Light and Co. Ltd.), after two crystallisations from nitrobenzene, had m. p. 207—209·5°.

3-*Nitro*-p-*terphenyl.*—4-Amino-3-nitro-*p*-terphenyl was prepared as described by Sawicki and Ray,[12] but with the following modifications. 4-Amino-*p*-terphenyl (18 g.) was *N*-propionylated by adding propionic anhydride (36 ml.), containing concentrated sulphuric acid (1 drop), to a boiling solution of the amine in propionic acid (360 ml.). The crude *product* (94%), m. p. 282—284·5°, was satisfactory for nitration. A sample (Found: C, 83·6; H, 6·6; N, 4·75. $C_{21}H_{19}NO$ requires C, 83·7; H, 6·35; N, 4·65%) separated from nitrobenzene or ethylene glycol monomethyl ether as a poorly crystalline solid, m. p. 282—285°. Fuming nitric acid (12 ml.; *d* 1·5) in acetic acid (75 ml.) was added during 2 min. to a stirred suspension of 4-propionamido-*p*-terphenyl (15 g.) in acetic acid (225 ml.) at 70°. After a total reaction time of 15 min., the mixture was cooled and the solid filtered off. The residue (92%), m. p. 197·5—198·5°, was satisfactory for deacylation. A sample (Found: C, 72·7; H, 5·4; N, 7·9. Calc. for $C_{21}H_{18}N_2O_3$: C, 72·9; H, 5·2; N, 8·1%) crystallised from acetic acid in yellow needles, m. p. 198·5—199°. In view of the discrepancy (27°) between this m. p. for 3-nitro-4-propionamido-*p*-terphenyl and that reported by Sawicki and Ray [12] (m. p. 171—172°), the constitution

[11] Paul, *J. Amer. Chem. Soc.*, 1958, **80**, 5332.
[12] Sawicki and Ray, *J. Org. Chem.*, 1954, **19**, 1903.

of the material above was proved by nitrating it in acetic acid, using the method for preparing 4,4″-dinitro-*p*-terphenyl from *p*-terphenyl.[3] The crude 3,4″-dinitro-4-propionamido-*p*-terphenyl (11%), isolated by dilution of the reaction mixture with a little water, was deacylated with boiling alcoholic sodium hydroxide, yielding 4-amino-3,4″-dinitro-*p*-terphenyl, m. p. 217·5—219°. A mixed m. p. with an authentic specimen [13] of the dinitro-amine was not depressed.

3-Nitro-4-propionamido-*p*-terphenyl (9 g.) in boiling ethylene glycol monoethyl ether (450 ml.) was treated with potassium hydroxide (3·6 g.) in water (4 ml.). After boiling for 2 min., the solution was cooled. Bright red crystals of 4-amino-3-nitro-*p*-terphenyl (89%), m. p. 269·5—271° (Found: C, 74·7; H, 5·1; N, 9·3. Calc. for $C_{18}H_{14}N_2O_2$: C, 74·5; H, 4·9; N, 9·65%), were obtained. Sawicki and Ray [12] report m. p. 271—272°. 4-Amino-3-nitro-*p*-terphenyl (6·37 g.) in acetic acid (45 ml.) was deaminated by the method described [13] for the preparation of 3,4″-dinitro-*p*-terphenyl. The orange paste was set aside for 60 min. before the addition of the hypophosphorous acid, after which the whole was kept at about 4° for 5 days and then at 20° for 12 hr. To isolate the 3-nitro-*p*-terphenyl, the filtrate from a suspension of the crude, dry product in benzene (300 ml.) was passed down a column of alumina (120 g.). The filter cake from the suspension was washed with benzene, and the washings were also placed on the column. The nitro-compound (4·5 g.) was eluted first (benzene eluate, 450 ml.). After crystallisation from a mixture of alcohol (400 ml.) and acetone (130 ml.), 3-*nitro*-p-*terphenyl* (3·84 g.) had m. p. 174—175°. The crystallisation liquors yielded a further 0·6 g. of material, m. p. 174°, a total yield of 74%. A sample (Found: C, 78·6; H, 4·5; N, 5·4. $C_{18}H_{13}NO_2$ requires C, 78·5; H, 4·8; N, 5·1%) crystallised from acetone as irregular, pale yellow plates, m. p. 176—176·5°.

*Proof of the constitution.* 3-Nitro-*p*-terphenyl (0·3 g.) was nitrated in acetic acid according to the method [3] used to prepare 4,4″-dinitro-*p*-terphenyl from *p*-terphenyl. Water (1 ml.) was added at the end of the reaction and crude 3,4″-dinitro-*p*-terphenyl (32%), m. p. 156·5—157·5°, was precipitated on cooling of the mixture. Crystallisation from benzene and then from acetic acid raised the m. p. to the constant value of 159—160·5°. A mixed m. p. with 3,4″-dinitro-*p*-terphenyl,[13] m. p. 161—162°, gave no depression.

*Amines.*—The most convenient means of preparing *small* amounts of 2-, 3-, and 4-amino-*p*-terphenyls is by the catalytic reduction of the nitro-compounds, as described below for reduction of the mixture of products obtained on mononitration of *p*-terphenyl. After removal of the ethyl acetate, the crude amines, obtained in almost quantitative yields, crystallised from alcohol. Pure 2′-nitro-*p*-terphenyl,[3] however, was incompletely reduced by the catalytic method after a reaction time of 3 hr. But, it should be noted that the catalytic reduction procedure was applied successfully to the quantitative reduction of mixtures of the nitro-compounds containing 2′-nitro-*p*-terphenyl. The success in these cases is explained by the low concentration of the 2′-nitro-isomer used in the synthetic mixtures chosen to simulate actual nitration products.

The pure 2′-isomeride (49%) was prepared by stannous chloride reduction of the nitro-compound.

2-Amino-*p*-terphenyl melted at 161—161·5°, agreeing with the m. p. of 159—160° reported by France, Heilbron, and Hey.[1] 2′-Amino-*p*-terphenyl (Found: C, 88·5; H, 6·75; N, 6·1. Calc. for $C_{18}H_{15}N$: C, 88·2; H, 6·2; N, 5·7%) had m. p. 175·5—176°. The benzoyl derivative (Found: C, 85·9; H, 5·4; N, 4·2. Calc. for $C_{25}H_{19}NO$: C, 85·9; H, 5·5; N, 4·0%), crystallised from alcohol, had m. p. 150°. Ames and Davey [14] report m. p.s of 171—172° and 148°, respectively, for these compounds. 3-*Amino*-p-*terphenyl* (79%) melted at 177—178° (Found: C, 88·2; H, 6·1; N, 5·8%). The amine (0·1 g.), acetic acid (2 ml.), and acetic anhydride (2 ml.) were refluxed for 15 min. Dilution with water gave 3-*acetamido*-p-*terphenyl*, m. p. 214—215° (from benzene) (Found: C, 83·6; H, 5·9; N, 4·9. $C_{20}H_{17}NO$ requires C, 83·6; H, 6·0; N, 4·9%). 4-Amino-*p*-terphenyl melted at 197—198°, giving a dark, misty melt. France, Heilbron, and Hey [1] report the same m. p. The acetyl derivative, from acetic acid, had m. p. 293—295° (lit.,[15] m. p. 294°).

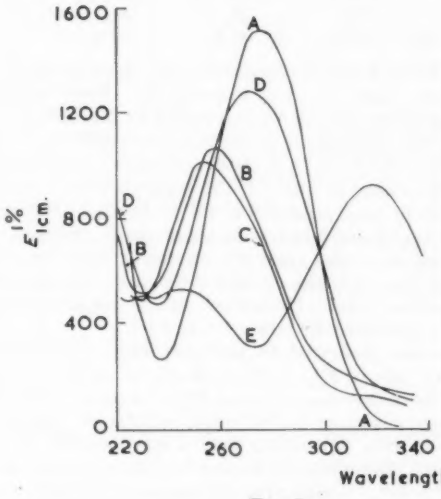
*Outline of Method of Analysis of Nitration Products.*—Complete mononitration of *p*-terphenyl gave a product contaminated with dinitro-compounds. Conditions were therefore chosen so

[13] Gray and Lewis, *J.*, 1961, 1069.
[14] Ames and Davey, *J.*, 1957, 3480.
[15] Pummerer and Bittner, *Ber.*, 1924, **57**, 84.

that only about 50% of the *p*-terphenyl underwent substitution. Since *p*-terphenyl yields the 2-, 2′-, and 4-isomerides on nitration,[2] such conditions result in the formation of a quaternary mixture. Nitration at the 3-position is discussed below.

Analyses of quaternary mixtures (prepared from the pure components) of known composition, by column chromatography on alumina, were unsatisfactory. It was also impracticable to use infrared (650—4000 cm.$^{-1}$) or near-infrared (1—2·8 μ) spectroscopy for the analyses as there were insufficient differences between the individual spectra. Furthermore, *p*-terphenyl and 4-nitro-*p*-terphenyl have extremely low solubilities in solvents suitable for infrared studies.

An ultraviolet spectrophotometric method was therefore developed. The instruments used were a Beckman DK-2 instrument equipped with an automatic pen recorder and a single-beam Uvispek instrument. Absorption spectra for the four compounds are shown in Fig. 1, and it is



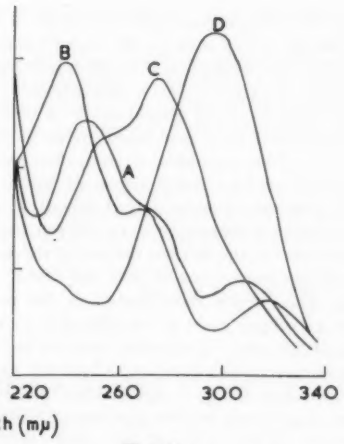




FIG. 1. FIG. 2.

FIG. 1. Ultraviolet spectra (A) *p*-terphenyl and its (B) 2-, (C) 2′-, (D) 3-, and (E) 4-nitro-derivative in cyclohexane.

FIG. 2. Ultraviolet spectra of (A) 2-, (B) 2′-, (C) 3-, and (D) 4-amino-*p*-terphenyl in cyclohexane.

obvious that there is little opportunity of distinguishing between 2- and 2′-nitro-*p*-terphenyl. However, it was possible to calculate the amounts of the hydrocarbon, 4-nitro-*p*-terphenyl, and (2 + 2′)-nitro-isomers present. The nitro-compounds were then reduced, and the quaternary mixture was digested with dilute hydrochloric acid. Basification of the extract yielded only the free amines which were analysed as a binary mixture of 2- and 2′-amino-*p*-terphenyl, since 4-amino-*p*-terphenyl hydrochloride has an extremely low solubility and the extract contained only traces of this isomer, for which a small correction was then applied.

*Calculation of the Isomer Ratios.*—The method given by Friedel and Orchin [16] was used to calculate the isomer ratios from the spectroscopic data. For a quaternary nitration mixture, the optical density of a solution (7—8 × 10$^{-4}$% w/v) in cyclohexane was measured at 254, 275, and 318 mμ (the wavelengths at which the 2′-nitro-isomer, the hydrocarbon, and the 4-nitro-isomer give strong absorption maxima). The composition of the binary amine mixture was similarly solved by measuring the optical density of a solution (7—8 × 10$^{-4}$% w/v) in cyclohexane at 230 and 260 mμ, and using the calibration spectra shown in Fig. 2.

*Accuracy of Results.*—The accuracy of the isomer ratios in Table 1 was checked in three ways.

[16] Friedel and Orchin, " Ultra-violet Spectra of Aromatic Compounds," Chapman and Hall, London, 1951, p. 29.

(i) Quaternary mixtures of known composition, prepared from the pure components, were treated as if they were nitration products. Table 4 summarises the results obtained from these synthetic mixtures.

TABLE 4.

| Expt. | | | Proportions of isomers (%) 2 | 2′ | 4 |
|---|---|---|---|---|---|
| | Theor. | | 26·7 | 13·3 | 60·0 |
| S 5 | Found | | 23 | 13 | 64 |
| S 6 | ,, | | 25 | 14 | 61 |
| | | Mean | 24 | 13·5 | 62·5 |
| | Theor. | | 40·0 | 20·0 | 40·0 |
| S 2 | Found | | 35 | 20 | 45 |
| S 3 | ,, | | 40 | 21 | 39 |
| S 4 | ,, | | 37 | 20 | 43 |
| | | Mean | 37·3 | 20·3 | 42·3 |

The two sets of synthetic mixtures in Table 4 may be considered as typical products from nitration in acetic acid at 20° and in acetic anhydride at 0° respectively. From the limited range of results available, it is indicated that a correction of 5% is required for the *ortho* (2- + 2′-) and *para* (4-) percentage compositions. The normalised percentage compositions of the 2- and 2′-isomers would then require a correction of 2%. If these corrections were justifiable on a statistical basis and were made to the results in Table 1, the general picture as regards the ratios of substitution at the *ortho*- and the *para*-positions in the molecule of *p*-terphenyl, under the various conditions of nitration, would not however be significantly changed.

(ii) The results from actual nitration mixtures (and synthetic mixtures) were also checked by determining the recovery, *i.e.*, the ratio of the sum of the calculated weights of the components in a mixture to the known weight of the mixture used. Quaternary and amine mixtures gave, respectively, recoveries of 95·2 and 100·2% (standard deviation 1·2 and 1·2).

(iii) The results were tested in the manner described by Cadogan, Hey, and Williams.[17] Amine mixtures gave a considerable error (about 8%) in the calculated absorption in the region of 295 mμ. This error was caused by an average of about 2% of 4-amino-*p*-terphenyl. The presence of this compound had not been considered in the initial calculation, and recalculation allowing for this isomer then gave a curve (X) having only a small scatter about the arithmetical mean of the percentage errors. Some typical results for the arithmetical mean are given: N 3, +1·7; N 14, +0·6; S 2, −0·7. Standard deviations were 0·7, 1·1, and 0·8, respectively. Any 3-nitro-*p*-terphenyl formed on nitration would arise as the free base in the amine mixture, and if present, should have been readily detected in curve X, especially in the region 270—300 mμ (cf. Fig. 2). Since there was no evidence for extraneous material, it can be taken that the amount of 3-nitro-*p*-terphenyl formed on nitration of *p*-terphenyl is too small for detection. The percentage error–wavelength curves were equally satisfactory for the quaternary mixtures. Some arithmetic means are quoted: N 2, −1·0; N 5, +2·4; S 5, +2·4. Standard deviations were 0·8, 2·1, and 2·2, respectively. The 3-nitro-isomer would in this case be more difficult to detect (cf. Fig. 1), since unchanged hydrocarbon might mask its presence.

*Nitration Procedure and Reduction of the Nitro-compounds to the Amines.*—The total volume of the nitration mixture, after addition of the fuming nitric acid to *p*-terphenyl (0·25 g.) dissolved in the appropriate solvent, was 385 ml. With acetic acid as solvent, nitration at 20° required 30 ml. of nitric acid, added as a solution of 1 part by vol. of nitric in 1 part of acetic acid (1 in 2 dilution). With acetic anhydride as solvent, nitration at 0°, 20°, 40°, and 80° required respectively, 1·0, 0·5, 0·3, and 0·4 ml. of nitric acid, added as a solution of 1 part of acid in 9 parts by vol. of acetic anhydride (1 in 10 dilution). After 24 hr., water (2·7 l.) was added and the suspension was placed in a refrigerator for 12 hr. in order to precipitate all the material. The product was then filtered off. For nitration in acetic anhydride, the addition of water gave two layers. This inhomogeneous mixture was set aside for 1 hr., then agitated to achieve a homogeneous aqueous phase which was then placed in a refrigerator. With either solvent, successful nitrations, *i.e.*, resulting in about 50% nitration of the *p*-terphenyl, gave a product having an upper m. p. of about 180°. A small portion was retained for spectroscopic determination of the ratio of nitration at the 4- and combined 2- and 2′-positions. The remainder (*ca.* 0·2 g.), dissolved in ethyl acetate (50 ml.), was reduced with

[17] Cadogan, Hey, and Williams, *J.*, 1954, 794.

hydrogen for 3—4 hr. at room temperature in the presence of Adams catalyst (0·01—0·015 g.). The catalyst was then filtered off and the fluorescent filtrate evaporated to dryness on a water bath. The residue was boiled for 30 min. with 1·2N-aqueous hydrochloric acid (25 ml.), and the suspended material filtered off while the mixture was hot. The filtrate was just neutralised with 2N-sodium hydroxide, and the precipitated amines (0·02—0·05 g.) were filtered off and washed once with water.

*Effect of Added Salts.*—(1) *Sodium nitrate.* *p*-Terphenyl was nitrated in acetic anhydride as described above, but the nitric acid, before dilution, contained dissolved anhydrous sodium nitrate. It was possible to correlate in a semiquantitative way the *upper* m. p. of a nitration product with the degree of nitration achieved. On use of nitric acid containing, before dilution, 0·0165M-nitrate, the products recovered from nitrations at 0° and 20° were both virtually unchanged *p*-terphenyl. Two experiments with nitric acid containing 0·000165M-nitrate gave, at 0°, products having upper m. p.s of 197° and 194°, *i.e.*, equivalent to about 22% nitration; and similarly at 20° the products had upper m. p.s of 204° and 200°, *i.e.*, equivalent to about 12% nitration. Nitration in acetic acid at 20° was similarly retarded by 0·000165M-nitrate (m. p. of product 197°).

(2) *Sodium perchlorate.* The m. p. of a product from a nitration in acetic anhydride or acetic acid which has resulted in about 50% nitration is 180—182°. On addition of 0·000165M-perchlorate to nitrations in acetic acid at 20°, acetic anhydride at 0°, and acetic anhydride at 20°, the m. p.s of the products were 181°, 180°, and 183°, *i.e.*, the degree of nitration was unaltered by the presence of the neutral salt.

The authors thank the Hull Local Education Authority for maintenance allowances to one of them (D. L.), the Distillers Co. Ltd. and Imperial Chemical Industries Limited for grants to the Department, and Dr. C. Daglish (Reckitt and Sons Ltd.) and his staff for the spectrophotometric determinations.

THE UNIVERSITY, HULL. [*Received, April 11th*, 1961.]

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## 1021. *Dipole Moments and Absorption Spectra of 4-Arylazo-1-naphthylamines.*

By D. A. IBBITSON, P. C. JAMES, and R. A. KNAUST.

Apparent dipole moments in benzene and dioxan, and ultraviolet absorption spectra of a series of 4-(*para*-substituted arylazo)-1-naphthylamines have been determined. The effect of the phenylazo-group is shown by comparing the moments with those of corresponding substituted anilines. The dipole moments determined in dioxan are all greater than those in benzene, indicating hydrogen bonding through the hydrogen atoms of the amino-group and the oxygen atom of the dioxan molecule. Interaction moments ($\mu_{int}$) along the C(ring)–N(amino) axis necessary to explain the observed moments have been evaluated, and show a trend parallel with the frequency of maximum absorption in the *Z*-band, half-wave potential, light fastness, and the Hammett σ-function for each of the substituents. It is suggested that these trends are all a measure of the effect of the *para*-substituent on the degree of conjugation between the azo-group and the aromatic ring system.

INVESTIGATIONS of the polarographic behaviour [1] of a series of 4-(*para*-substituted arylazo)-1-naphthylamines indicate a linear relation between the half-wave potential, $E_{\frac{1}{2}}$, and the Hammett σ-function [2] for each of the substituents. The substituent groups cause electron displacements at the azo-linkage with resulting changes in the electron affinity of the molecule, the slope of the linear plot indicating that electron-attracting groups favour reduction.

Atherton and Seltzer,[3] and Atherton and Peters,[3] measured the rate of fading of the

[1] Catchpole and Knaust, *J.*, 1960, 4241.
[2] Hammett, *J. Amer. Chem. Soc.*, 1937, **59**, 96.

arylazo-1-naphthylamines, in terms of a quantity $k$, the destruction efficiency, a low value of which corresponds to a high light-fastness. These authors claimed that their results were in accord with a reaction mechanism in which the dye molecule, excited by light absorption, was oxidised by the air, the nitrogen atoms of the azo-group acting as electron donors.

Dipole moments and ultraviolet absorptions are now reported, and found to be consistent with polarography and light-fastness data, and with the Hammett substituent constant.

Dipole moments determined in benzene and dioxan, and calculated as described previously,[4] are summarised in Table 1, where $\alpha$ and $\nu$ are the limiting values of $d\varepsilon/dw$ and $dn^2/dw$, respectively, and the other symbols have their usual significance.

TABLE 1.

Polarisation data for solutions of 4-(*para*-substituted arylazo)-1-naphthylamines at 25°.

| Subst. | Solv.* | $10^3\alpha$ | $10^3\nu$ | $P_\infty$ (c.c.) | $\mu$ (D) | Subst. | Solv.* | $10^3\alpha$ | $10^3\nu$ | $P_\infty$ (c.c.) | $\mu$ (D) |
|---|---|---|---|---|---|---|---|---|---|---|---|
| MeO ... | B | 2450 | 98 | 75·9 | 1·93 | Br ..... | B | 6033 | 114 | 299·3 | 3·83 |
| MeO ... | D | 5325 | 134 | 175·5 | 2·93 | Br ..... | D | 8975 | 111 | 416·9 | 4·52 |
| Me ..... | B | 2033 | 104 | 47·9 | 1·53 | $MeO_2C$ | B | 5700 | 104 | 266·4 | 3·61 |
| Me ..... | D | 3925 | 131 | 106·9 | 2·29 | $MeO_2C$ | D | 10,400 | 132 | 449·5 | 4·69 |
| H ..... | B | 3429 | 93 | 115·7 | 2·38 | Ac ..... | B | 11,750 | 101 | 583·4 | 5·34 |
| H ..... | D | 5775 | 120 | 181·3 | 2·97 | Ac ..... | D | 17,050 | 163 | 725·9 | 5·96 |
| Cl ..... | B | 6367 | 122 | 271·9 | 3·65 | | | | | | |
| Cl ..... | D | 10,550 | 143 | 416·2 | 4·51 | | | | | | |

* B = Benzene; D = dioxan.

In agreement with other workers,[5] it is found that, since these amino-compounds are capable of hydrogen bonding through the hydrogen atoms of the amino-group and the oxygen atom of the dioxan molecule, the dipole moments determined in dioxan are all greater than those in benzene. The greater differences between the apparent moments in dioxan and benzene of the arylazo-1-naphthylamines than those, in parentheses, for the corresponding substituted anilines [5d] may be due to enhancement of the $+M$ effect of the amino-group by the increased length of the conjugated system in the former compounds; H 0·59 (0·24), Me 0·76 (0·18), Cl 0·86 (0·38), Br 0·69 (0·35). Also, in this connection, it is noteworthy that the apparent moments in benzene of the arylazo-1-naphthylamines are all greater than those of the corresponding substituted anilines (Table 2).

Introduction of a *p*-methoxy-group in aniline causes an increase in the apparent moment from 1·53 to 1·80 D, whereas a decrease in moment from 2·38 to 1·93 D occurs when this group is substituted in phenylazo-1-naphthylamine. The same effect is observed with the following compounds: *NN*-dimethylaniline (1·55 D),[6] *p*-methoxy-*NN*-dimethylaniline (1·70 D),[6] 4-amino-*NN*-dimethylazobenzene (3·22 D),[7] 4-amino-4′-methoxy-*NN*-dimethylazobenzene (2·77 D).[7] Campbell, Young, and Rogers [7] suggest that the difference in moment of the last two compounds arises from contributions, to the resonance state of the 4′-methoxy-compound, of structures of the type $Me{\cdot}O^+{:}C_6H_4{:}N{\cdot}N^-{\cdot}C_6H_4{\cdot}NMe_2$. A similar explanation is possible for the effect of the methoxy-group when substituted in phenylazo-1-naphthylamine. In addition to the methoxy-group, the methyl group is electron-releasing and on substituting this group in phenylazo-1-naphthylamine a decrease in moment from 2·38 to 1·53 D is observed. The same effect occurs on substituting the methyl group in the 4′-position in 4-amino-*NN*-dimethylazobenzene, the decrease in

[3] Atherton and Seltzer, *J. Soc. Dyers and Colourists*, 1949, **65**, 629; Atherton and Peters, *ibid.*, 1952, **68**, 64.

[4] Erić, Goode, and Ibbitson, *J.*, 1960, 55.

[5] (*a*) Vassiliev and Syrkin, *Acta Physicochim. U.R.S.S.*, 1941, **14**, 414; (*b*) Few and Smith, *J.*, 1949, 753; 1949, 2663; (*c*) Smith, *J.*, 1950, 3532; 1953, 109; (*d*) Smith and Walshaw, *J.*, 1957, 3217

[6] Hertel and Dumont, *Z. phys. Chem.*, 1935, *B*, **30**, 139.

[7] Campbell, Young, and Rogers, *J. Amer. Chem. Soc.*, 1951, **73**, 5789.

TABLE 2.

| Substituent | H | *p*-Cl | *p*-Br | *p*-Me | *p*-$MeO_2C$ | *p*-Ac | *p*-MeO |
|---|---|---|---|---|---|---|---|
| $\mu$ (D) (arylazo-1-naphthylamine deriv.) | 2·38 | 3·65 | 3·83 | 1·53 | 3·61 | 5·34 | 1·93 |
| $\mu$ (D) (aniline deriv.) ..... | 1·53[a] | 3·01[a] | 3·01[a] | 1·32[a] | — | 4·48[b] | 1·80[c] |

[a] Ref. 5*d*. [b] Curran and Estok, *J. Amer. Chem. Soc.*, 1950, **72**, 4575. [c] Williams and Fogelberg, *J. Amer. Chem. Soc.*, 1930, **52**, 1356.

TABLE 3.

| Subst. | $\mu_{int}$ | $\sigma$ † | $E_{\frac{1}{2}}$ (v) at pH = 5·1 | $k$ * (mean values) | $10^{-3}\bar{\nu}_1$ (cm.$^{-1}$) | $10^{-3}\bar{\nu}_2$ (cm.$^{-1}$) | Previous values [15] $10^{-3}\bar{\nu}_2$ (cm.$^{-1}$) |
|---|---|---|---|---|---|---|---|
| OMe ..... | 1·40 | −0·268 | −0·455 | 0·25 | 34·7 | 23·0 | 22·99 |
| Me ..... | 1·04 | −0·170 | −0·429 | 0·13 | 34·6 | 22·9 | 22·73 |
| H ..... | 1·44 | 0·000 | −0·410 | 0·00 | 34·7 | 22·7 | 22·83 |
| Cl ..... | 1·49 | 0·227 | −0·389 | −0·37 | 34·5 | 21·8 | 21·83 |
| Br ..... | 1·52 | 0·232 | −0·381 | −0·33 | 34·4 | 21·5 | |
| $CO_2Me$ ..... | 2·05 | 0·636 | −0·366 | −0·66 | 34·1 | 20·5 | |
| Ac ..... | 2·09 | 0·874 | −0·308 | −0·38 | 33·9 | 20·3 | |

* $k$ = log of the ratio of the destruction efficiencies of the substituted and unsubstituted compound.

† $\sigma$ = Hammett's substituent constant.

moment being from 3·22 to 2·75 D. Again, contributions from structures similar to that suggested for the methoxy-substituted compounds may occur, due to hyperconjugation of the methyl group with the azo-linkage.

Apparent dipole moments in benzene and dioxan of aniline,[5b] 1-naphthylamine,[8] 4-aminoazobenzene,[9] and 4-phenylazo-1-naphthylamine are 1·51 (1·75), 1·49, 2·43 (3·04), and 2·38 D (2·97 D), respectively, values in dioxan being given in parentheses. These moments suggest that replacement of a benzene by a naphthalene residue only slightly affects the polarity of the molecule. Therefore, a C(ring)–$NH_2$ group moment in dioxan of 1·75 D and moments of 1·50 D [5d] and 0·37 D for *p*-toluidine and toluene, respectively, were assumed, and the angle which the C(ring)–$NH_2$ group moment in aniline makes with the C(ring)–N(amino) axis was calculated vectorially by Marsden and Sutton's method [10] to be 42° 49′. By assuming also that this angle remains unchanged in 4-phenylazo-1-naphthylamine, additional moments ($\mu_{int}$) along the C(ring)–N(amino) axis, necessary to explain the observed moments in dioxan of the arylazo-1-naphthylamines have been calculated from equation 1:

$$\mu_{obs}^2 = 1{\cdot}75^2 + (\mu_{int} + \mu_{PhX})^2 + 2(1{\cdot}75)(\mu_{int} + \mu_{PhX}) \cos 42° 49' \qquad (1)$$

The following values have been taken for the moments of the parent monosubstituted benzenes ($\mu_{PhX}$): chlorobenzene 1·58, bromobenzene 1·56, toluene −0·37.

In the case of those arylazo-1-naphthylamines with angular substituents, the angles ($\alpha$) which the substituent group moments make with a direction parallel to the C(ring)–N(amino) bond have been calculated vectorially from the following dipole moments: anisole [5d] 1·23, *p*-methylanisole [5d] 1·20, toluene 0·37 ($\alpha$ = 76° 40′); acetophenone [11] 2·96, 4-methylacetophenone [11] 3·23, toluene 0·37 ($\alpha$ = 134° 22′); methyl benzoate [8] 1·83, methyl *p*-toluate [8] 2·04, toluene 0·37 D ($\alpha$ = 119° 58′). The values of $\mu_{int}$ have been computed from the vector diagram (Fig. 1), free rotation of the two vectors about the direction of the C(ring)–N(amino) axis being assumed. Results are recorded in Table 3.

The absorption spectrum of azobenzene shows an intense band at 31450 cm.$^{-1}$ which has been ascribed to conjugation between the azo-group and the aromatic ring system.[12] *para*-Substituted azobenzenes exhibit a bathochromic shift in the absorption spectra,

[8] Wesson, "Tables of Electric Dipole Moments," Technology Press, Cambridge, Mass., 1948.
[9] Ibbitson, Jackson, McCarthy, and Stone, *J.*, 1960, 5127.
[10] Marsden and Sutton, *J.*, 1936, 599.
[11] Bentley, Everard, Marsden, and Sutton, *J.*, 1949, 2957.
[12] Burawoy, *J.*, 1939, 1177.

and Sawicki,[13] from a study of a series of substituted *NN*-dialkylaminoazobenzenes, concluded that conjugation of the *p'*-substituent with the substituted amino-group is important in bringing about this bathochromic shift. This type of band structure involving zwitterionic resonance structures is called the *Z* band.[14] Examination of the absorption spectra of the arylazo-1-naphthylamines, determined within the range 40,000—15,000 cm.$^{-1}$, reveals two pronounced absorption maxima at frequencies $\tilde{\nu}_1$ and $\tilde{\nu}_2$ (Table 3). We attribute frequencies $\tilde{\nu}_2$ to the *Z* band, an absorption maxima for phenylazo-1-naphthylamine at 22,700 cm.$^{-1}$ corresponding to Turner's value [15] of 22,830 cm.$^{-1}$. As in the case of azobenzene derivatives, substitution of electron-acceptor groups in a position of conjugation in the benzene ring decreases the energy of the zwitterionic structures. The energy change involved in the transition from ground to excited state is decreased, and

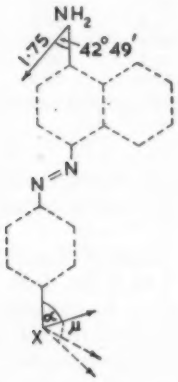


FIG. 1. Calculation of $\mu_{int}$ for 4-*p*-methoxyphenylazo-1-naphthylamine, 4-*p*-acetylphenylazo-1-naphthylamine, and 4-*p*-methoxycarbonylphenylazo-1-naphthylamine.

X = MeO; $\alpha = 76° 40'$; $\mu = 1{\cdot}23$ D.
X = Ac; $\alpha = 134° 22'$; $\mu = 2{\cdot}96$ D.
X = $MeO_2C$; $\alpha = 119° 58'$; $\mu = 1{\cdot}83$ D.

the wavelength maximum of the band system shows the expected bathochromic shift. Although the value for the methoxyl group is anomalous, $\Delta\mu_{int}(\mu_{sub} - \mu_{unsub})$ may be regarded as a measure of the tendency of the *p'*-substituent to withdraw electrons from the azo-group. The greater this tendency, the more readily will reduction occur, and the more difficult it will be for oxidation to occur at the azo-group. Again, the frequency shift $\Delta\tilde{\nu}_2$ is greater the more powerful the electron-accepting property of the substituent group. From the results in Table 3, therefore, it appears that, in general, the trends in $\mu_{int}$, $\tilde{\nu}_2$, $E_{\frac{1}{2}}$, and $k$ are all a measure of the effect of the *p'*-substituent groups on the degree of conjugation between the azo-group and the aromatic ring system.

## EXPERIMENTAL

*Materials.*—The 4-arylazo-1-naphthylamines were prepared from the anilines by diazotisation and coupling with 1-naphthylamine, followed by recrystallisation to constant m. p. Dioxan and benzene were repeatedly refluxed with sodium and then fractionally distilled under anhydrous conditions.

*Methods and Results.*—Absorption spectra were determined on a Unicam S.P. 700 instrument with 10 mm. cells, the concentration of the solutions of the azo-compounds in absolute alcohol being $5 \times 10^{-5}$M.

Dielectric constants and refractive indices of solutions of graded concentration of each azo-compound in benzene and dioxan were determined at 25° by the same methods and in the same apparatus as in a previous investigation.[4] Dielectric constants were calculated

[13] Sawicki, *J. Org. Chem.*, 1957, **22**, 915.
[14] Sawicki, *J. Org. Chem.*, 1956, **21**, 605.
[15] Turner, *J.*, 1949, 2282.

TABLE 4.

| 100*w* | ε | $n_D$ | 100*w* | ε | $n_D$ | 100*w* | ε | $n_D$ | 100*w* | ε | $n_D$ |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 4-Phenylazo-1-naphthylamine | | | | | | 4-*p*-Chlorophenylazo-1-naphthylamine | | | | | |
| in benzene | | | in dioxan | | | in benzene | | | in dioxan | | |
| 0·000 | 2·2725 | 1·4981 | 0·000 | 2·2113 | 1·4198 | 0·000 | 2·2725 | 1·4981 | 0·000 | 2·2114 | 1·4198 |
| 0·226 | 2·2800 | 1·4988 | 0·049 | 2·2138 | 1·4200 | 0·118 | 2·2797 | 1·4986 | 0·047 | 2·2163 | — |
| 0·451 | 2·2882 | 1·4995 | 0·094 | 2·2168 | 1·4202 | 0·171 | 2·2833 | 1·4988 | 0·121 | — | 1·4204 |
| 0·677 | 2·2957 | 1·5002 | 0·290 | 2·2282 | 1·4211 | 0·227 | 2·2866 | 1·4990 | 0·195 | 2·2323 | 1·4208 |
| 0·899 | 2·3033 | 1·5009 | 0·387 | 2·2336 | 1·4214 | 0·284 | 2·2907 | 1·4992 | 0·291 | — | 1·4213 |
| | | | | | | 0·340 | 2·2942 | 1·4995 | 0·295 | 2·2427 | — |
| | | | | | | | | | 0·397 | 2·2530 | 1·4218 |
| 4-*p*-Bromophenylazo-1-naphthylamine | | | | | | 4-*p*-Tolylazo-1-naphthylamine | | | | | |
| in benzene | | | in dioxan | | | in benzene | | | in dioxan | | |
| 0·000 | 2·2725 | 1·4981 | 0·000 | 2·2098 | 1·4198 | 0·000 | 2·2725 | 1·4981 | 0·000 | 2·2135 | 1·4198 |
| 0·111 | 2·2795 | 1·4985 | 0·047 | 2·2142 | 1·4200 | 0·115 | 2·2747 | 1·4985 | 0·047 | 2·2153 | 1·4200 |
| 0·166 | 2·2829 | 1·4987 | 0·095 | 2·2182 | 1·4202 | 0·170 | 2·2760 | 1·4987 | 0·098 | 2·2175 | 1·4203 |
| 0·227 | 2·2857 | 1·4990 | 0·202 | 2·2278 | 1·4206 | 0·231 | 2·2773 | 1·4989 | 0·199 | 2·2214 | 1·4207 |
| 0·284 | 2·2892 | 1·4992 | 0·282 | 2·2352 | 1·4209 | 0·282 | 2·2782 | 1·4991 | 0·291 | 2·2250 | 1·4211 |
| 0·340 | 2·2930 | 1·4994 | 0·401 | 2·2458 | 1·4214 | 0·341 | 2·2793 | 1·4993 | 0·388 | 2·2284 | 1·4216 |
| 4-*p*-Acetylphenylazo-1-naphthylamine | | | | | | 4-*p*-Methoxycarbonylphenylazo-1-naphthylamine | | | | | |
| in benzene | | | in dioxan | | | in benzene | | | in dioxan | | |
| 0·000 | 2·2725 | 1·4981 | 0·000 | 2·2117 | 1·4198 | 0·000 | 2·2725 | 1·4981 | 0·000 | 2·2117 | 1·4198 |
| 0·114 | 2·2857 | 1·4985 | 0·028 | 2·2165 | 1·4200 | 0·110 | 2·2791 | 1·4985 | 0·098 | 2·2217 | 1·4202 |
| 0·171 | 2·2927 | 1·4987 | 0·050 | 2·2205 | — | 0·169 | 2·2823 | 1·4987 | 0·192 | 2·2313 | 1·4207 |
| 0·227 | 2·2995 | 1·4989 | 0·074 | — | 1·4202 | 0·226 | 2·2850 | 1·4989 | 0·295 | 2·2423 | 1·4212 |
| 0·283 | 2·3052 | 1·4991 | 0·096 | 2·2282 | — | 0·282 | 2·2882 | — | 0·386 | 2·2520 | 1·4216 |
| | | | 0·121 | — | 1·4205 | 0·339 | 2·2920 | 1·4993 | 0·482 | 2·2619 | 1·4220 |
| | | | 0·193 | 2·2444 | — | | | | | | |
| | | | 0·200 | 2·2462 | 1·4210 | | | | | | |
| 4-*p*-Methoxyphenylazo-1-naphthylamine | | | | | | | | | | | |
| in benzene | | | in dioxan | | | | | | | | |
| 0·000 | 2·2725 | 1·4981 | 0·000 | 2·2135 | 1·4198 | | | | | | |
| 0·104 | 2·2750 | — | 0·187 | 2·2235 | 1·4207 | | | | | | |
| 0·368 | 2·2814 | 1·4993 | 0·256 | 2·2270 | — | | | | | | |
| 0·553 | 2·2859 | 1·4999 | 0·376 | 2·2333 | 1·4216 | | | | | | |
| 0·785 | 2·2916 | 1·5007 | 0·462 | 2·2382 | — | | | | | | |
| 1·026 | 2·2975 | — | 0·553 | 2·2428 | 1·4224 | | | | | | |
| | | | 0·756 | — | 1·4233 | | | | | | |

relative to the value of 2·2725 at 25° for pure benzene. The results are recorded in Table 4, where the symbols have their usual significance.

We thank Mr. J. Hall for assistance in the preparations, Mr. N. W. Vale for the construction of the heterodyne-beat apparatus, D.S.I.R. for a grant for the purchase of a Unicam S.P. 700 instrument, the Joint Education Committee for the Derby and District College of Art and Technology for the award of a Research Assistantship (to R. A. K.), and Dr. A. G. Catchpole for discussions.

DERBY AND DISTRICT COLLEGE OF TECHNOLOGY. [*Received, May 4th,* 1961].

## 1022. *Estimation of the Relative Amounts of Isomeric Sulphate Esters in Some Sulphated Polysaccharides.*

By D. A. Rees.

It is shown that suitably linked L-galactose 6-sulphate units in porphyran can be converted quantitatively by alkaline treatment into 3,6-anhydrogalactose. This treatment has been used to estimate the proportion of this sulphate in the polysaccharide, the conclusion being confirmed by periodate oxidation and infrared studies. The present sample of porphyran contains 9·8% of sulphate (as $SO_3$) of which 86% is present as 1,2- or 1,4-linked L-galactose 6-sulphate. The mucilage of *Dilsea edulis* has been re-examined by these techniques, and an earlier structure is revised to accommodate the new findings. Certain other galactan sulphates have been briefly examined.

The eliminations of carbohydrate sulphates in alkaline solution were elucidated by Percival,[1] and the principles were subsequently applied quite widely [2,3] in attempts to deduce the positions of sulphate ester groups in polysaccharides from the stability of the esters to alkali. Unfortunately, precautions were not usually taken in such structural work to avoid the release of sulphate by general destruction of the polysaccharide under the strongly alkaline conditions (usually boiling N-sodium hydroxide), and the results give at most a qualitative answer. When a proportion of the ester is labile to alkali it is often uncertain whether this is due to degradation of the polysaccharide or to more specific $S_N2$ elimination with resultant anhydro-ring formation.[1] The results of such studies have therefore been conclusive only when the new sugar units could be identified,[3a] or when it could be shown that the ester was so placed that it could not be eliminated. Methods have now been devised whereby alkaline elimination can be exploited more fully for the structural analysis of some seaweed polysaccharides.

Porphyran, the galactan sulphate of the marine red alga *Porphyra umbilicalis*,[4] was used as a model because it contains L-galactose 6-sulphate units which are so linked that according to Percival's rules the ester should be labile to alkali, giving 3,6-anhydrogalactose.[5] In preliminary experiments, the 3,6-anhydrogalactose present in the reaction mixture was measured, as an indication of the extent of both sulphate elimination and polysaccharide degradation. The reaction proceeded at a convenient rate in N-sodium hydroxide at 80°, but was attended by rapid destruction of the polysaccharide (Table, *a*).

Concentration of 3,6-anhydrogalactose (% of initial value) on treatment of porphyran with alkali.

| Time (min.) | 40 | 70 | 130 | 170 | 200 | 260 | 300 |
|---|---|---|---|---|---|---|---|
| 3,6-Anhydrogalactose (% of initial value) from: | | | | | | | |
| (*a*) porphyran | 148 | 152 | 126 | | 109 | | |
| (*b*) reduced porphyran | 172 | 186 | | 186 | | 177 | |
| (*c*) reduced porphyran + borohydride | | 193 | 215 | | 215 | | 215 |

Destruction of the polysaccharide was substantially less when porphyran was reduced with potassium borohydride before the reaction (Table, *b*), suggesting that the principal cause of degradation was " peeling " from the reducing end.[6] The fact that slight destruction occurred even after reduction indicated a certain amount of depolymerisation, probably exposing new reducing groups at which " peeling " could occur. This secondary degradation was avoided by including potassium borohydride in the actual reaction mixture,

[1] Percival, *Quart. Rev.*, 1949, **3**, 369.
[2] Buchanan, Percival, and Percival, *J.*, 1943, 51; Conchie and Percival, *J.*, 1950, 827; Fisher and Percival, *J.*, 1957, 2666.
[3] Barry and Dillon, *Proc. Roy. Irish Acad.*, 1945, **50**, *B*, 349.
[3a] Ricketts, *J.*, 1956, 3752; Overend and Ricketts, *Chem. and Ind.*, 1957, 632.
[4] Peat, Turvey, and Rees, *J.*, 1961, 1590; Turvey and Rees, *Nature*, 1961, **189**, 831.
[5] Rees, *Biochem. J.*, 1961, **81**, 347.
[6] Whistler and BeMiller, *Adv. Carbohydrate Chem.*, 1958, **13**, 289.

the new reducing groups presumably being protected under these conditions by immediate reduction (Table, *c*). The properties of the product isolated from the reaction confirmed that degradation had been minimised. It was non-dialysable, gave more viscous solutions than the original porphyran, and exhibited a tendency to gel out of solution (especially in the presence of salts) which was not shown by the original porphyran. The sulphate content was diminished (1·9%; originally 9·8%) and the anhydrogalactose content increased (30·0%; originally 12·9%). The product therefore resembles agar and κ-carrageenin in its high 3,6-anhydrogalactose content and in its tendency to form gels. Also there was molar correspondence between the sulphate released and the anhydro-sugar formed (104% recovery of 3,6-anhydrogalactose), confirming that all the sulphate release involved 3,6-anhydride formation.

These results cannot be used with confidence to calculate the proportion of 6-sulphate in porphyran, because 3,6-anhydrogalactose could also be given by galactose 3-sulphate units with a free position 6. However, only those 3,6-anhydrogalactose-producing units in which the sulphate is at position 6 will be attacked by periodate. It was found that porphyran reduced, on average, 0·40 mole of periodate for every hexose unit, and that when the oxidised polysaccharide was warmed with alkali under the usual conditions no increase in the 3,6-anhydrogalactose content was observed. It therefore seems that all the sugar sulphate residues giving rise to the 3,6-anhydride are in fact oxidised by periodate, *i.e.*, are 1,2- or 1,4-linked L-galactose 6-sulphate units, the L-configuration following because it has been established [4] that all the 6-sulphate, if not all the sulphate, is attached to L-galactose units.

The infrared spectrum of porphyran showed absorption bands thought to be characteristic of sulphate esters.[7] These were at 1240 (given by all sulphate esters), 820 (given by sulphated primary hydroxyl groups), and 850 cm.$^{-1}$ (given by sulphated secondary hydroxyl groups which are axial with respect to the sugar ring to which they are attached). The absorption at 820 cm.$^{-1}$ was strong, as would be expected since this represents (from the above evidence) at least 86% of the ester. This peak was absent from the alkali-treated porphyran, confirming once more that 6-sulphate was removed in 3,6-anhydrogalactose formation. The 850 cm.$^{-1}$ absorption was weak and was present in porphyran both before and after alkaline treatment, consistently with its having arisen from galactose 4-sulphate units which are stable to alkali in whatever glycosidic linkage.

These experiments show that 86% of the ester sulphate in this sample of porphyran is present as 1,2- or 1,4-linked L-galactose 6-sulphate, the 1,4-linkage being, for reasons already stated,[5] the more likely. The remainder of the sulphate might be attached to position 4 of galactose units, though further evidence for this is desirable. The content of L-galactose 6-sulphate is sufficient to account for 70% of the periodate uptake, so that most of the other units are apparently joined by 1,3-linkages. Since it has been shown that L-galactose 6-sulphate is probably the biological precursor of the 3,6-anhydrogalactose in native porphyran,[5] these two units are likely to be structurally equivalent, and taken together they represent one-third to one-half of the sugar units in the polysaccharide. A distinct resemblance therefore emerges between porphyran and certain other polysaccharides of the red algae, which contain approximately equal amounts of 1,3-linked D-galactose and 1,4-linked 3,6-anhydrogalactose, sometimes with position 4 of the D-galactose units sulphated.[8]

*The Mucilage of* Dilsea edulis.—Although a tentative structure has been put forward for this polysaccharide,[9] the previous authors emphasised that more work is necessary before a unique structure is possible. The evidence quoted concerning the location of

[7] Orr, *Biochim. Biophys. Acta*, 1954, **14**, 173; Lloyd, Dodgson, Price, and Rose, *ibid.*, 1961, **46**, 108; Lloyd and Dodgson, *ibid.*, p. 116.
[8] (*a*) O'Neill, *J. Amer. Chem. Soc.*, 1955, **77**, 6324; Araki, *Bull. Chem. Soc. Japan*, 1956, **29**, 543; (*b*) Yaphe, *Canad. J. Bot.*, 1959, **37**, 751.
[9] Barry and McCormick, *J.*, 1957, 2777.

XUM

the sulphate groups has been that (i) much of the ester is stable to alkali since " 50% of the combined sulphate is retained after 13 hours' boiling," [3] (ii) an unidentified relatively acid-stable substance, which gives 3,6-anhydrogalactosazone with phenylhydrazine, is present in the hydrolysate of the polysaccharide.[9] Barry and McCormick [9] pointed out that these two phenomena could be explained if the polysaccharide contained 1,3-linked galactose 6-sulphate units, since according to Percival's rules such a unit would be stable to alkali and some of the free sugar 6-sulphate would survive the conditions used for acidic hydrolysis to give 3,6-anhydrogalactosazone on subsequent treatment with phenylhydrazine. When the mucilage of *Dilsea edulis* was re-examined the following points emerged: (i) There is pronounced infrared absorption at 850 cm.$^{-1}$, with none detectable at 820 cm.$^{-1}$; it therefore appears that most of the sulphate is on galactose units at position 4. (ii) Warming the material with alkali increases the amount of 3,6-anhydrogalactose in the solution by an amount corresponding to 6% of the total sulphate, similar treatment of the oxidised polysaccharide leading to no such increase. A modification of Barry and McCormick's structure such as the following is therefore necessary. Two structurally dissimilar regions exist,[9] and these may be in the same or different molecules. The major component is a chain of 1,3-linked galactopyranose units (with the possibility of some branching), sulphate occurring on positions 4 of some of these. This structure takes account of the results of the Barry degradation studies by the earlier workers and explains the infrared results and the alkali-stability of most of the sulphate; this structure is similar to that of the λ-carrageenin studied by Morgan and O'Neill.[10] The second region is an alternating chain of 1,3- and 1,4-linked galactose units, some of the 1,3-linked units perhaps carrying sulphate at position 4 and some of these linked 1,4 occurring as the 6-sulphate or 3,6-anhydride. Xylose was originally supposed to occur in this region, but it now appears that this was part of a contaminating polysaccharide, since it is only present in traces in the present sample (purified by precipitation with Cetavlon). In the absence of further evidence the uronic acid is not placed in either region. This second structure is also a revision of that formerly put forward on the basis of Barry degradation studies; it accounts for the results of the present alkali and periodate studies and for the indications of 6-sulphate found by Barry and McCormick. It resembles that of certain other red seaweed polysaccharides (see the discussion of porphyran above).

*Other Polysaccharides.*—λ-Carrageenin has also been studied in this way: the preliminary results have been published.[11] Certain other seaweed polysaccharides, when warmed with alkali, showed small increases in 3,6-anhydrogalactose content, the extent corresponding in each case to the release of 2—5% of the total sulphate. Structural significance cannot be given to these observations until the homogeneity of the samples has been more closely examined, but together with the results already reported they show that units giving 3,6-anhydrogalactose on warming with alkali are common in the galactan sulphates of red algae. The specimens examined were: κ-carrageenin,[8] the water-soluble polysaccharides of *Eucheuma spinosum*, and the polysaccharides precipitated by potassium ions from extracts of *Furcellaria fastigiata* [12] and *Hypnea musciformis*.[8b] In all cases the infrared spectrum suggested, by the existence of a band at 850 cm.$^{-1}$, that the major sulphate ester was galactose 4-sulphate.

## Experimental

The sample of porphyran, except where otherwise stated, was prepared by Mr. T. P. Williams, working in collaboration with Professor Stanley Peat, F.R.S., and Dr. J. R. Turvey, by extraction of seaweed harvested in June. It had 9·8% of sulphate (as $SO_3$) and 12·9% of 3,6-anhydrogalactose (anhydro-basis).

*Analytical Methods.*—Infrared spectra of polysaccharides were recorded with a Perkin–Elmer Infracord spectrophotometer and Nujol mulls. 3,6-Anhydrogalactose was determined

[10] Morgan and O'Neill, *Canad. J. Chem.*, 1959, **37**, 1201.
[11] Rees, *Chem. and Ind.*, 1961, 793.
[12] Painter, *Canad. J. Chem.*, 1960, **38**, 112; Clancy, Walsh, Dillon, and O'Colla, *Proc. Roy. Dublin Soc.*, 1960, **1**, *A*, 197.

by Yaphe's resorcinol method.[13] Determinations of total ester sulphate were carried out by destruction of the sample (about 1 mg.) with concentrated nitric acid at 100° in a sealed tube overnight, in the presence of sodium chloride (1 mg.). The nitric acid was boiled off and the last traces were removed by co-evaporation with concentrated hydrochloric acid, the residue was dissolved in water (1 ml.), and the sulphate determined spectrophotometrically with 4-amino-4′-chlorodiphenyl.[14]

*General Procedure for Alkaline Treatment of Polysaccharides and Oxidised Polysaccharides.*—The material, in 0·2—1·0% aqueous solution, was reduced with an excess of potassium borohydride at room temperature for 24 hr., and 3N-sodium hydroxide (0·5 vol.) was added together with a further quantity of potassium borohydride (about twice the weight of polysaccharide). A sample was withdrawn into a Pyrex test-tube which was sealed and heated on a water-bath at 80° for 2—4 hr. The tube was opened (care is necessary, because the tube contains hydrogen under pressure, which tends to ignite if the tube is opened by applying the molten tip of a glass rod to a scratch), and the 3,6-anhydrogalactose present in the contents compared with that in the remainder of the solution which had been kept at room temperature. In control experiments no change in 3,6-anhydrogalactose content was detected when such solutions were kept at room temperature for 24 hr. In examination of periodate-oxidised polysaccharides the reagents were re-calibrated with standards containing the same amount of iodide as the unknown, since iodide interferes slightly with the method.

*Large-scale Alkaline Treatment of Porphyran.*—Porphyran (1·61 g.) in water (250 ml.) was reduced at room temperature for 48 hr. with potassium borohydride (0·2 g.). Sodium hydroxide (10 g.) and potassium borohydride (3 g.) were dissolved in the solution, and the flask loosely stoppered and placed on a water bath at 80° for 2 hr. After this period the 3,6-anhydrogalactose content had risen to a value corresponding to 28·0% of the original material. The alkaline solution was neutralised (Amberlite IR-120 resin, $H^+$ form) and a portion placed in a dialysis bag in a beaker of stirred water. No 3,6-anhydrogalactose-containing material had passed through the membrane after 24 hr. (limit of detection, 1% of the amount present). The viscous solution was dialysed exhaustively against running tap water (3 days) and freeze-dried (1·24 g.; 1·87% of sulphate and 30·0% of 3,6-anhydrogalactose). From the analytical figures it is calculated that 1·61 millimoles of ester sulphate were eliminated in the reaction, with concomitant formation of 1·69 millimoles of 3,6-anhydrogalactose.

*Periodate Oxidation of Porphyran.*—Porphyran (16·9 mg.) was dissolved in 0·04M-sodium metaperiodate (10 ml.) and left in the dark at room temperature, the change in periodate concentration being followed spectrophotometrically.[15] Samples (1 ml.) were withdrawn into ethylene glycol (3 drops) for determination of residual galactose 6-sulphate by the method given above. The following results were obtained:

| | | | |
|---|---|---|---|
| Time (hr.) ..... | 27 | 50 | 120 |
| Periodate consumed (mole per hexose unit) ..... | 0·31 | 0·35 | 0·40 |
| Galactose 6-sulphate remaining (%) ..... | 19 | 12 | 0 |

*Examination of the Mucilage of* Dilsea edulis.—This sample was kindly given by Drs. K. O. Lloyd and P. F. Lloyd. It was recovered from the residues from floridean starch preparation.[16] It had 0·9% of 3,6-anhydrogalactose and 15·0% of sulphate. Only traces of xylose were detected by paper chromatography of a complete acid hydrolysate. Treatment with alkali was carried out by the general method given above. The mucilage (12 mg.) was oxidised at room temperature in the dark in 0·05M-periodate (2·5 ml.). After 4 days, 94% of the units which originally gave 3,6-anhydrogalactose with alkali had been removed.

*Other Polysaccharides.*—The other polysaccharides mentioned in the discussion were kindly provided by Dr. W. Yaphe.[8b,13]

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West Mains Road, Edinburgh, 9. [*Received, June 15th,* 1961.]

[13] Yaphe, *Analyt. Chem.*, 1960, **32**, 1327.
[14] Jones and Letham, *Chem. and Ind.*, 1954, 662.
[15] Aspinall and Ferrier, *Chem. and Ind.*, 1957, 1216.
[16] Peat, Turvey, and Evans, *J.*, 1959, 3223.

XUM

## 1023. *Reactions at Position 1 of Carbohydrates. Part II.*[1] *The Variation of Optical Rotation of Some Aryl Glucosides with Temperature.*

By B. Capon, W. G. Overend, and M. Sobell.

The temperature coefficients of optical rotation (sodium D-line) of some aryl D-glucopyranosides and their tetra-*O*-acetyl derivatives have been measured. With the exceptions of *o*-nitrophenyl α- and β-D-glucopyranoside and tetra-*O*-acetyl-β-D-glucopyranoside all the compounds examined showed only slight dependence of optical rotation on temperature. Possible causes of the large temperature-dependence for the three above-named glucosides are discussed.

An exception to Hudson's second isorotation rule [2] was noted by Montgomery *et al.*[3] who found that the $2B_{Ac}$ value calculated from the observed optical rotations of the *o*-nitrophenyl tetra-*O*-acetyl-D-glucopyranosides was high owing to the anomalous positive rotation of the β-anomer. [Values for the *m*- and *p*-nitrophenyl glucoside acetates were unexceptional.] The result was confirmed by Pigman [4] who showed in addition that the acetylated 2,4- and 2,6-dinitrophenyl β-D-glucopyranosides had anomalous positive rotations. He found that these high rotations decrease rapidly on elevation of temperature and at 150° they approach the values expected from application of Hudson's rules. The effect also occurs in the D-galactoside series since Snyder and Link [5] showed that *o*-nitrophenyl tetra-*O*-acetyl-β-D-galactopyranoside also has an anomalous positive rotation and a high variation of optical rotation with temperature. Further they

Table 1.

2,3,4,6-Tetra-*O*-acetyl derivatives of aryl β-D-glucosides.

| Aglycone | M. p. | $[\alpha]_D$ in $CHCl_3$ ($c$) | Literature values: M. p. | Literature values: $[\alpha]_D$ in $CHCl_3$ | Ref. |
|---|---|---|---|---|---|
| *Group A* | | | | | |
| *o*-Nitrophenyl | 159—161° | +43·2° (1·98) | 160·5—161·5° | +43·0° | *A* |
| *o*-Chlorophenyl | 149—151 | −50·2 (1·02) | 149—150 | −51·6 | *B* |
| *o-Bromophenyl* * | 149—151 | −53·7 (1·0) | — | — | |
| *o*-Iodophenyl | 159—161 | −57·4 (1·0) | 154—155 | −48·2 | *C* |
| 1-Naphthyl | 177—178 | −76·4 (0·5) | 178—179 | −72 | *D* |
| *Group B* | | | | | |
| *o*-Acetylphenyl | 150—152 | −49·9 (0·97) | 151—152·5<br>148—150 | —<br>−43 | *E*<br>*F* |
| *o*-Methoxycarbonylphenyl | 158—159 | −31·1 (1·0) | 160·5 | −29·3 | *G* |
| 2,6-*Dibromophenyl* † | 132—134 | −8·0 (1·0) | — | — | — |
| *Group C* | | | | | |
| Phenyl | 125—126 | −22·5 (1·0) | 124—125 | −22·0 | *D* |
| 2-Naphthyl | 134—135 | −20·2 (3·0) | 135—136 | −19 | *D* |
| *p*-Bromophenyl | 132—133 | −18·5 (2·9) | 133 | −17·8 | *H* |
| *m*-Chlorophenyl ‡ | 112—114 | −21·8 (1·1) | 131·5—133·5<br>112·5 | −22·8<br>−25·3 | *B*<br>*I* |

* Found: C, 48·1; H, 4·65; Br, 15·8; Ac, 34·0. $C_{20}H_{23}BrO_{10}$ requires C, 47·7; H, 4·6; Br, 15·9; Ac, 34·2%. † Found: C, 41·0; H, 3·9; Br, 27·6. $C_{20}H_{22}Br_2O_{10}$ requires C, 41·3; H, 3·8; Br, 27·5%. ‡ Recryst. from methanol.

Refs.: (*A*) Latham, May, and Mosettig, *J. Org. Chem.*, 1950, **15**, 884. (*B*) Nath and Rydon, *Biochem. J.*, 1954, **57**, 1. (*C*) Jermyn, *Austral. J. Chem.*, 1955, **8**, 403. (*D*) Helferich and Schmitz-Hillebrecht, *Ber.*, 1933, **66**, 378. (*E*) Jerzmanowska and Markiewicz, *Roczniki Chem.*, 1956, **30**, 59. (*F*) Helferich, Scheiber, Streeck, and Vorsatz, *Annalen*, 1935, **518**, 211. (*G*) Helferich and Lutzmann, *Annalen*, 1939, **537**, 11. (*H*) Hurd and Bonner, *J. Amer. Chem. Soc.*, 1945, **67**, 1764. (*I*) Bonner, Kubitshek, and Drisko, *J. Amer. Chem. Soc.*, 1952, **74**, 5082.

[1] Part I, Overend, Peacocke, and Smith, *J.*, 1961, 3487.
[2] Hudson, *J. Amer. Chem. Soc.*, 1909, **31**, 66.
[3] Montgomery, Richtmyer, and Hudson, *J. Amer. Chem. Soc.*, 1942, **64**, 690.
[4] Pigman, *J. Res. Nat. Bur. Stand.*, 1944, **33**, 129.
[5] Snyder and Link, *J. Amer. Chem. Soc.*, 1953, **75**, 1758.

demonstrated that *o*-nitrophenyl β-D-gluco-, β-D-galacto-, and α-L-arabino-pyranoside have temperature coefficients of optical rotation of the same order of magnitude as their fully acetylated derivatives, but in each case the optical rotation increased rather than decreased with increase of temperature.

Pigman considered that steric interaction between the *o*-nitro-group and the substituents attached to the asymmetric centres of the pyranoid ring was probably responsible for such anomalous effects. At room temperature these interactions would prevent the molecule from assuming some of the conformations which it could take up in the absence of the *o*-nitro-substituent in the aglycone, and if each conformation makes a contribution to the optical rotation an anomalous value would be expected. At higher temperatures thermal energy would counteract the steric interactions and the optical rotation would change to a value more in accord with expectation. In the present work this problem has been examined further and the temperature coefficients of optical rotation of a number of *ortho*-substituted aryl D-glucopyranosides have been measured.

TABLE 2.

Aryl D-glucopyranosides.

| Aglycone | M. p. | $[\alpha]_D$ (*c* in $H_2O$) | Literature values M. p. | Literature values $[\alpha]_D$ ($H_2O$) | Literature values Ref. | Periodate uptake[n] (mol.) |
|---|---|---|---|---|---|---|
| *α-Anomers* | | | | | | |
| *p*-Nitrophenyl ..... | 213—215° | +222° (0·42) | 216° | +215° | 3 | 1·90 |
| *o*-Nitrophenyl ..... | 184—186 | +228 (0·46) | 186—188 | +206 | 3 | 1·89 |
| *β-Anomers* | | | | | | |
| Phenyl ..... | 172—173 | −73·7 (0·92) | 175—176 | −71·9 | *J* | 1·88 |
| | | | 171—172 | — | *B* | |
| 2-Naphthyl (+$H_2O$)[m] | 188—190 | — | 188 | −26·7 (95% $Me_2CO$) | *K* | 1·87 |
| ,, (anhyd.)[a] | 191—192 | −77·3 (0·73 in 96% EtOH) | 183 | −88 | *C* | |
| p-*Bromophenyl* | | | | | | |
| (+$H_2O$)[b] ..... | 179—181 | — | — | — | — | |
| (anhyd.)[c] ..... | 179—181 | −69·9 (1·0) | — | — | — | 1·86 |
| m-*Chlorophenyl* | | | | | | |
| (+2$H_2O$)[d] ..... | 179—181 | — | — | — | — | 1·94 |
| (anhyd.)[e] ..... | 179—181 | −85 (0·5) | 179—180 | −36·3 | *B* | |
| *o*-Nitrophenyl..... | 169—171 | −116 (0·64) | 168—170 | −140·4 | *B* | 1·80 |
| | | | 152 | −106 | 3 | |
| *o*-Aminophenyl[f] ..... | 174—176 | −70·3 (0·93) | 183·5—184·5 | −71·2 | *A* | — |
| *o*-Chlorophenyl ..... | 170—171 | −80·7 (0·63) | 170—171 | −90·6 | *B* | 1·76 |
| *o*-*Bromophenyl*[g] ..... | 149—150 | −65 (0·9) | — | — | — | 1·87 |
| *o*-Iodophenyl[h] ..... | 162—163 | −58·5 (1·1) | 156 | −48·5 | *C* | 1·83 |
| 1-*Naphthyl*[i] ..... | 174—175 | −94·3 (0·68) | — | — | — | 1·84 |
| *o*-Acetylphenyl[j] ..... | 152—153 | −66 (0·98) | 152—154 | −66·5 | *F* | 1·81 |
| *o*-Methoxycarbonyl-phenyl[k] ..... | 106—108 | −67·7 (0·89) | 107 | −64·4 | *G* | 1·84 |
| 2,6-*Dibromophenyl*[l] ... | 176—178 | ±0 (0·5) −2·0 (96% EtOH) | — | — | — | 1·79 |

[a] Obtained by heating the monohydrate *in vacuo* over phosphoric oxide at 120°. [b] Found: C, 41·4; H, 4·8; $H_2O$, 3·95. $C_{12}H_{15}BrO_6,0·75H_2O$ requires C, 41·3; H, 4·8; $H_2O$, 3·9%. [c] Obtained by heating the hydrate at 110° *in vacuo* over phosphoric oxide (Found: C, 43·1; H, 4·5; Br, 24·1. $C_{12}H_{15}BrO_6$ requires C, 43·0; H, 4·5; Br, 23·8%). [d] Found: C, 44·3; H, 6·1; $H_2O$, 11·0. $C_{12}H_{15}ClO_6,2H_2O$ requires C, 44·1; H, 5·9; $H_2O$, 11·0%. [e] Obtained by heating the dihydrate at 110° *in vacuo* over phosphoric oxide (Found: C, 49·7; H, 5·1; Cl, 12·0. Calc. for $C_{12}H_{15}ClO_6$: C, 49·6; H, 5·2; Cl, 12·2%). [f] Recryst. from ethyl acetate–ethanol. The literature constants refer to a hydrate of composition $C_{12}H_{17}NO_6,0·75H_2O$. [g] Found: C, 43·2; H, 4·5; Br, 23·2%. [h] Recryst. from ethanol. [i] Found: C, 62·8; H, 5·95. $C_{16}H_{18}O_6$ requires C, 62·7; H, 5·9%. Recryst. from ethyl–acetate ethanol. [j] Recryst. from ethyl acetate–ethanol. [k] Recryst. from ethanol. [l] Recryst. from ethanol–water (Found: C, 34·9; H, 3·4; Br, 38·3. $C_{12}H_{14}Br_2O_6$ requires C, 34·8; H, 3·4; Br, 38·6%). [m] Recrystallised from ethanol–water. [n] Formaldehyde was not produced in any of the oxidations.

Refs.: *A—G*, see Table 1. (*J*) Fischer and von Mechel, *Ber.*, 1916, **49**, 2813. (*K*) Robertson and Waters, *J.*, 1930, 2729.

The compounds examined are listed in Tables 1 and 2. They were prepared according to the methods outlined in the Experimental section. That the aryl D-glucosides listed in Table 2 had the pyranoside structure was proved by periodate oxidation (see Table 2).

The optical rotations were measured over a range of about 50° and for all the compounds studied the specific rotations were plotted against temperature, yielding good straight lines. The rates of variation of specific rotation per degree Centigrade were calculated from the slopes of these lines. These rates were corrected for the rates of change of optical rotation arising from concentration changes on expansion of the solvent by means of the known temperature-variation of the densities of the solvents. These corrected values are shown in Table 3.

TABLE 3.

Temperature-dependence of optical rotation.

| Aglycone | $d[\alpha]_D/dT$ for acetylated D-glucopyranoside in $(CHCl_3)_2$ | $d[\alpha]_D/dT$ for D-glucopyranoside in water | Aglycone | $d[\alpha]_D/dT$ for acetylated D-glucopyranoside in $(CHCl_3)_2$ | $d[\alpha]_D/dT$ for D-glucopyranoside in water |
|---|---|---|---|---|---|
| *α-Anomer* | | | *β-Anomer* | | |
| *o*-Nitrophenyl... | +0·021°(0·50) | −0·67° (0·45) | *m*-Chlorophenyl | +0·033°(1·99) | +0·14° (0·50) |
| *p*-Nitrophenyl... | +0·044 (0·49) | −0·17 (0·40) | *p*-Bromophenyl | +0·033 (2·00) | +0·08 (1·00) |
| *β-Anomer* | | | 2,6-Dibromophenyl ..... | −0·003 (2·00) | 0·00 (0·50) |
| Phenyl ..... | +0·023 (1·50) | +0·065 (0·92) | *o*-t-Butylphenyl | +0·042 (1·50) | +0·085 * (1·03) |
| *o*-Nitrophenyl... | −0·37 (2·02) | +0·72 (0·63) | *o*-Methoxycarbonylphenyl... | +0·061 (0·99) | +0·15 (0·89) |
| *o*-Aminophenyl | +0·052 (1·51) | +0·10 (0·945) | *o*-Acetylphenyl | +0·007 (1·49) | +0·11 (0·98) |
| *o*-Chlorophenyl | +0·034 (1·50) | +0·13 (0·63) | 1-Naphthyl ... | +0·025 (1·00) | +0·12 (0·68) |
| *o*-Bromophenyl | +0·020 (1·49) | +0·11 (0·90) | 2-Naphthyl ... | +0·023 (2·01) | +0·046 † (0·725) |
| *o*-Iodophenyl ... | +0·041 (1·50) | +0·093 (1·11) | | | |

* Solvent: 50% (v/v) aqueous ethanol. † Solvent: 96% (w/w) aqueous ethanol.
The values in parentheses are concentrations.

With the exceptions of *o*-nitrophenyl 2,3,4,6-tetra-*O*-acetyl-β-D-glucoside and 2,6-dibromophenyl 2,3,4,6-tetra-*O*-acetyl-β-D-glucoside, all the acetylated aryl β-D-glucopyranosides examined showed a change in optical rotation to a less negative value on heating from room temperature to 70°. The changes are all approximately similar in magnitude to that of phenyl tetra-*O*-acetyl-β-D-glucopyranoside in which the aglycone is unsubstituted. The specific rotations of 2,6-dibromophenyl β-D-glucopyranoside and its tetra-acetate both showed negligible change on elevation of temperature. The result obtained for *o*-nitrophenyl tetra-*O*-acetyl-β-D-glucopyranoside was similar to that reported by Pigman [4] who used nitrobenzene as solvent. Variation in the nature or site of substitution of the halogen atom in monohalogenophenyl β-D-glucopyranoside or the tetra-*O*-acetate had no significant effect on the temperature coefficient of optical rotation. Although 1-naphthyl tetra-*O*-acetyl-β-D-glucopyranoside has a high (negative) specific rotation (−72·5°) at room temperature, when the glycoside was heated the change in rotation proceeded at a rate similar to that for the corresponding unsubstituted phenyl glycoside. Both *o*- and *p*-nitrophenyl tetra-*O*-acetyl-α-D-glucopyranoside showed normal rates of variation of optical rotation with temperature.

The optical rotations of all the aryl β-D-glucopyranosides studied, except 2,6-dibromophenyl β-D-glucopyranoside, became less negative with increasing temperature. Apart from *o*-nitrophenyl β-D-glucopyranoside the rates of variation of specific rotation of these compounds were all of the same magnitude. (As with the corresponding acetylated compounds the largest rate was found for *o*-methoxycarbonylphenyl β-D-glucoside.) *o*-Nitrophenyl β-D-glucopyranoside gave a large temperature variation of specific rotation which was in good agreement with that given by Snyder and Link.[5] (Our value of 0·72° per degree Centigrade can be compared with a value of 0·75° obtained when Snyder and Link's results are corrected for density changes.)

Pigman and Isbell [6] have pointed out that when a group which is *meta*-directing in aromatic electrophilic substitution is substituted in the aglycone of phenyl β-D-glucopyranoside the molecular rotation of the *para*-isomer is appreciably greater than that of the *ortho*-form (see Table 4). At higher temperatures we find that the nitro-group follows the pattern shown by other *meta*-directing groups at room temperature. Also, at the higher temperatures the values of the molecular rotations of *o*- and *p*-nitrophenyl β-D-glucoside tend towards those found for other *meta*-directing groups at room temperature. Therefore, like its acetylated derivative *o*-nitrophenyl β-D-glucopyranoside has an unusually high rotation at room temperature.

TABLE 4.

Molecular rotations of some substituted phenyl β-D-glucopyranosides.[6]

| Subst. | $CO_2H$ | $CO_2Me$ | $CH_2{\cdot}CN$ | Ac | CHO | $NO_2$ at 20° | $NO_2$ at 70° |
|---|---|---|---|---|---|---|---|
| *ortho*-Posn. ... | −18,400° | −20,200° | −19,700° | −19,800° | −18,000° | −34,900° | −24,100° |
| *para*-Posn. ... | −24,400° | −24,500° | −21,000° | −28,100° | −26,900° | −32,200° | −29,800° * |

* Calc. by extrapolation of the results cited in ref. 5.

From these results it appears that the anomaly under discussion cannot arise entirely from steric interaction resulting from the presence of a large substituent in the *ortho*-position of the aglycone (cf. Pigman [4] and Snyder and Link [5]). If this were the true explanation replacement of the nitro-substituent by a t-butyl, acetyl, methoxycarbonyl, or iodo-group would not be expected greatly to alter the anomaly. In fact it destroys the effect. A large group located *ortho* to a nitro-group causes it to be twisted out of the plane of the benzene ring.[7] An asymmetric group (*e.g.*, glucosyl) would induce further asymmetry into the molecule as the nitro-group would be more likely to be twisted one way than the other. This could be a possible cause of the anomalous optical rotation of the *o*-nitrophenyl glycosides. In this case, on increase of temperature steric interactions would be reduced and the optical rotatory behaviour would become normal. It is difficult, however, to reconcile this explanation with the results obtained with some of the other *ortho*-substituted glycosides. It is difficult to escape the conclusion that the reason for the odd behaviour of the *o*-nitrophenyl glycosides resides in some property of the nitro-group, other than shape or size. It may be that the powerful N–O dipole results in an interaction between the nitro-group and the sugar moiety. This interaction would be repulsive if it were between the nitro-group and the C–O dipole of an acetate group, but attractive if between a nitro-group and a hydroxyl group. It will be recalled that *o*-nitrophenyl glucopyranoside and its tetra-acetate differ in the sign of the temperature coefficients of optical rotation. In the present state of knowledge, however, this explanation must remain speculative.

## EXPERIMENTAL

*Aryl Tetra-O-acetyl-β-D-glucopyranosides.*—The majority of the compound are listed in Table 1. The glycosides in group A were obtained by heating together (under reflux for 4—6 hr.) tetra-*O*-acetyl-α-D-glucopyranosyl bromide, an excess of potassium carbonate, and a slight excess of the appropriate phenol in anhydrous acetone. The products were precipitated by addition of water and cooling to 0°, and recrystallised from ethanol or ethanol–acetone. The compounds in group B were prepared by cooling and triturating a mixture of tetra-*O*-acetyl-α-D-glucopyranosyl bromide (0·025 mol.), the appropriate phenol (0·03 mol.), silver oxide (0·022 mol.), and quinoline (0·08 mol.). After storage in a desiccator for 30 min. with stirring every 10 min. the mixture was extracted with glacial acetic acid (40 ml.). In each case the product was precipitated by pouring the extract into water (400 ml.) at 0° and was recrystallised from ethanol. The tetra-acetates in group C were synthesised by heating penta-*O*-acetyl-β-D-glucopyranose (0·075 mol.), the phenol (0·32 mol.), and toluene-*p*-sulphonic acid

[6] Pigman and Isbell, *J. Res. Nat. Bur. Stand.*, 1941, **27**, 9.
[7] See M. Wepster in "Progress in Stereochemistry," ed. by Klyne and de la Mare, Butterworths Scientific Publ., London, 1958, Vol. II, pp. 99—156.

(1 g.) at 110°/15 mm. for 1·5 hr. Benzene (200 ml.) was added and the solution was washed successively with water, several times with 10% sodium hydroxide, and water. The benzene layer was dried ($Na_2SO_4$) and evaporated at 15 mm. to give a residue which recrystallised from ethanol. *o*-t-Butylphenyl 2,3,4,6-tetra-*O*-acetyl-β-D-glucoside, m. p. 189—191°, $[\alpha]_D^{23}$ −34·7° (*c* 0·98 in $CHCl_3$) {Nath and Rydon [8] give m. p. 191°, $[\alpha]_D^{22}$ −34·8° (in $CHCl_3$)}, was prepared similarly except that heating was prolonged to 2 hr. and the excess of *o*-t-butylphenol was removed by distillation *in vacuo* as it is not very soluble in alkali. *o*-Aminophenyl 2,3,4,6-tetra-*O*-acetyl-β-D-glucoside (78%), m. p. 131—133°, $[\alpha]_D^{21}$ −34·1° (*c* 1·1 in MeOH), −26·9° (*c* 1·0 in $CHCl_3$) {Latham *et al.*[9] give m. p. 132—133°, $[\alpha]_D^{20}$ −33·9° (in MeOH)}, was prepared by the reduction of *o*-nitrophenyl tetra-*O*-acetyl-β-D-glucopyranoside (3 g.) in 1,4-dioxan (100 ml.) at room temperature and atmospheric pressure with hydrogen and Raney nickel. The product was isolated in standard manner and recrystallised from ethanol.

*Aryl Tetra*-O-*acetyl*-α-D-*glucopyranosides*.—*o*- and *p*-Nitrophenyl 2,3,4,6-tetra-*O*-acetyl-α-D-glucoside {m. p. 101—103°, $[\alpha]_D^{20}$ +178° (*c* 0·49 in $CHCl_3$), and m. p. 109—110°, $[\alpha]_D^{24}$ +170·4° (*c* 0·21 in $CHCl_3$) respectively} were prepared by heating penta-*O*-acetyl-α-D-glucopyranose (0·075 mol.) and the nitrophenol (0·35 mol.) with zinc chloride (7 g.) in a mixture (22 ml.) of acetic anhydride (5 vol.) and acetic acid (95 vol.) at 125° for 1 hr. under a vacuum. Benzene (200 ml.) was added and the solution was washed successively with water, 5% sodium hydroxide solution (several times), and water. Evaporation of the dried ($Na_2SO_4$) benzene layer afforded a syrup which was triturated and recrystallised from ethanol. An attempt to prepare *o*-chlorophenyl 2,3,4,6-tetra-*O*-acetyl-α-D-glucoside by this route (except that the reaction was not carried out under reduced pressure) yielded the β-isomer. If the time of heating was increased to 1·5 or 4 hr., only oily products could be isolated. Likewise, when *o*-bromophenol was used with this method, only the β-form of *o*-bromophenyl 2,3,4,6-tetra-*O*-acetyl-D-glucoside was obtained.

*Aryl* D-*Glucopyranosides*.—The aryl tetra-*O*-acetyl-D-glucopyranosides were deacetylated in methanol by the Zemplén–Pacsu procedure. The compounds listed in Table 2 were obtained. Except where indicated the products were recrystallised from water. *o*-t-Butylphenyl β-D-glucoside was obtained only in syrupy form, $[\alpha]_D^{20}$ −58·5° (*c* 1·0 in 50% EtOH–$H_2O$).

*Periodate Oxidations*.—The glycosides were oxidised with 0·015M-sodium metaperiodate and the uptake of oxidant was measured according to Aspinall and Ferrier's procedure.[10] The results are shown in Table 2. The glycosides were then oxidised with the reagent according to O'Dea and Gibbons's method [11] to determine whether formaldehyde was produced in the reaction.

*Solvent*.—Technical *sym*-tetrachloroethane was distilled over sodium hydrogen carbonate, and the fraction, b. p. 145—148°, was collected and stored over sodium hydrogen carbonate.

*Procedure*.—The optical rotations were measured with a Hilger polarimeter with a sodium lamp as light source. Lagged 2 dm. jacketed polarimeter tubes were used, through which water from a thermostat (control to ±0·2°) was circulated. The initial temperature of the solution (20·0° or 25·0°) was increased by steps of 5° to a final value of 70°. To measure the temperature of the solution a thermometer was inserted through the centre-filling aperture of the polarimeter tube. When equilibrium was reached for each temperature, the thermometer was removed and the rotation of the solution recorded. The rotation of every solution studied always returned to within ±0·01° of its initial value, when the solution was cooled to room temperature, showing that the process is completely reversible.

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[8] Nath and Rydon, *Biochem. J.*, 1954, **57**, 1.
[9] Latham, May, and Mosettig, *J. Org. Chem.*, 1950, **15**, 884.
[10] Aspinall and Ferrier, *Chem. and Ind.*, 1957, 1216.
[11] O'Dea and Gibbons, *Biochem. J.*, 1953, **55**, 580.

## 1024. *Glow-discharge Electrolysis. Part IV.*[1] *The Formation of Hydrazine in Liquid Ammonia.*

By A. Hickling and G. R. Newns.

The glow-discharge electrolysis of electrolyte solutions in liquid ammonia has been investigated over a wide range of conditions. The main product in solution is hydrazine in amount dependent upon the quantity of electricity passed. The yield initially when the glow-discharge electrode is an anode is 2·5 moles/faraday, but it decreases somewhat as hydrazine accumulates in the solution and a stationary concentration of about 2M is ultimately reached; the hydrazine yield is substantially independent of most other experimental variables. It is considered that the reactions are initiated by positively charged gaseous ions which are accelerated in the cathode fall near the liquid surface. On entering the liquid phase these are involved in both charge- and energy-transfer reactions producing $NH_2$ radicals. The proportions of the products formed are then considered to depend upon the competition of the various possible reactions of these radicals, and on this basis a quantitative interpretation of the results is possible.

In the previous parts of this series [1] the glow-discharge electrolysis of a variety of aqueous electrolytes has been investigated. It has been shown that, with the anode in the vapour phase, current is carried to the liquid surface by gaseous ions.[2] These are accelerated in the cathode fall of approximately 415 v which occurs within 0·05 cm. of the water surface, and they enter the solution with energies which the experimental results suggest are of the order of 100 ev. Thus in addition to bringing about oxidation by charge transfer, they may also cause dissociation of water molecules, and the process is analogous to the action of an ionising radiation where the energies of the bombarding particles are relatively small but where the dose rate can be extremely high. The experimental results agree with a scheme whereby 7—8 equivalents of OH radical are formed for each faraday of electricity passed, and the proportions of the products formed depend upon the competition of the various possible reactions of these radicals.

The present investigation was undertaken to extend the work to a non-aqueous solvent, and liquid ammonia was selected as providing a convenient system of considerable intrinsic interest. Preliminary work showed [3] that the main product formed was hydrazine, and its production has been comprehensively studied and the mechanism of the process investigated.

### Experimental

The cell used is shown in Fig. 1. It consisted of a large Pyrex test tube topped by a B34 socket. This connected it to a head through which anode and cathode were introduced by B14 joints, and which led through a spiral reflux condenser to a vacuum system containing a float manostat so that the pressure in the apparatus could be maintained constant over long periods. The anode was a platinum wire and the cathode was a small sheet of platinum foil, and they were so arranged that with a given volume of solution in the cell the cathode was completely immersed and the anode was a predetermined distance above the liquid surface. To maintain a constant temperature the cell was surrounded by a vacuum flask containing a suitable coolant, usually solid carbon dioxide in alcohol, and this was also used in the reflux condenser above the cell.

Current was supplied by a Leland rectifier unit of adjustable voltage (0—1500 v) through a suitable ballast resistance (5000—9000 Ω), a calibrated milliameter, and a gas coulometer. The discharge was initiated by a pulse from an induction coil; once started it required about

[1] Parts I—III, Davies and Hickling, *J.*, 1952, 3595; Hickling and Linacre, *J.*, 1954, 711; Denaro and Hickling, *J. Electrochem. Soc.*, 1958, **105**, 265.
[2] Dewhurst, Flagg, and Watson, *J. Electrochem. Soc.*, 1959, **106**, 366.
[3] Hickling and Newns, *Proc. Chem. Soc.*, 1959, 368.

600 v and the current could be maintained steady at any desired value between 0·01 and 0·1 A. Various electrolytes have been used in this work; that most commonly employed was 0·01M-ammonium nitrate, and it was made by adding the appropriate volume of liquid ammonia to a weighed quantity of the " AnalaR " salt. Liquid ammonia was usually used direct from the cylinder; in some experiments it was purified by distillation from sodium and introduced into the cell without exposure to air, but the results were not appreciably different from those obtained with the commercial product which contains a little water. The standard experimental conditions employed except where otherwise stated were: electrolyte, 20 ml. of 0·01M-solution of ammonium nitrate in liquid ammonia, exposing a surface of 9 sq. cm.; anode to surface distance, 0·5 cm.; pressure, 100 mm. mercury; temperature of the electrolyte, *ca.* −75°; current, 0·025 A; voltage drop across the discharge, *ca.* 600 v.

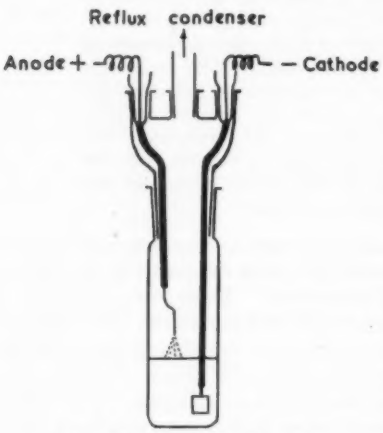


FIG. 1. Electrolytic cell.

The usual experimental procedure was to pass known quantities of electricity under different conditions and subsequently to analyse the solution and to express the yields of products in moles/faraday; the quantity of electricity passed was accurately measured by a hydrogen–oxygen voltameter of the Lingane type. Preliminary investigation [3] showed that the main product in the liquid phase was hydrazine. This was identified by its reducing properties, precipitation as sulphate, reaction with salicylaldehyde, colour reaction with *p*-dimethylaminobenzaldehyde, and isolation by fractional distillation as a liquid of m. p. 1·0—1·5°, with vapour pressure of 10·5 mm. at 20° and $n_D^{22}$ 1·4609. Other conceivable products such as azides, nitrites, hydroxylamine, and hydrogen peroxide (in the presence of water) were tested for but were not normally found. The conditions for separation and exact estimation of the hydrazine were carefully worked out. It was found desirable to distil out the bulk of the ammonia slowly from the sample to be analysed, and to acidify the residue with sulphuric acid while a little ammonia remained. The resulting solution was diluted to a known volume and the hydrazine present estimated either volumetrically by the indirect iodate method, or colorimetrically with a Spekker absorptiometer and the *p*-dimethylaminobenzaldehyde reagent. Good agreement was given by the two methods.

## RESULTS

*Physical Features of the Discharge.*—The discharge was a sharply defined yellow cone with the apex at the anode tip and the base in the liquid surface. Its physical characteristics were explored with the anode at various distances up to 1 cm. from the solution surface, with the pressure varied in the range 70 to 230 mm., and with currents of 0·006 to 0·1 A. The overall voltage between the anode and the solution increased linearly with rise of pressure and increase of anode distance, and it fell slightly with rise of current for electrode–solution distances greater than about 0·3 cm.; for smaller separations the negative voltage–current characteristic became positive. Over the whole range of conditions the total voltage across the discharge varied between a minimum of 470 and a maximum of 750 v. The potential distribution within the discharge was investigated by using a thin wire probe and valve voltmeter, and it was found that there was a potential difference of 390 v across a distance of 0·06 cm. from the liquid surface. In contrast to the total voltage, this cathode fall was largely independent of experimental variables such as current, electrode distance, and gas pressure, and it compares with a value of 415 v found for a similar cathode fall when aqueous solutions are used.[1]

The area of the luminous spot in the liquid surface was also measured over a range of conditions. It increased with increasing anode distance and with decrease in gas pressure; it also increased with increasing current in such a way that the current density (c.d.) fell slightly. The latter is a parameter of importance since the concentration of any reactive species formed

in the reaction zone is likely to depend upon it. Under the standard experimental conditions the area of the glow spot was 0·13 sq. cm. and the c.d. in it was 0·19 A/sq. cm. It is noteworthy that over the whole range of conditions explored, the variation of c.d. was relatively small; its minimum value was 0·13 and its maximum value 0·38 A/sq. cm.

*Chemical Effects of the Discharge.—Influence of general factors.* (*a*) Quantity of electricity. The graph of yield of hydrazine in moles against quantity of electricity passed in faradays for a series of electrolyses under the standard conditions for various times has been previously shown.[1] The initial yield was approximately 2·5 moles of hydrazine/faraday of electricity passed, and this fell slightly as hydrazine accumulated in the electrolyte. It seems clear that two processes are occurring: initial formation of hydrazine in amount proportional to the quantity of electricity passed, and decomposition of hydrazine dependent upon its concentration in the solution. It is convenient for this reason to distinguish between the instantaneous or differential yield of hydrazine, as given by a tangent to the formation curve, and the integrated yield for the passage of a definite quantity of electricity; thus the differential yield at the beginning of electrolysis gives the rate of formation of hydrazine in moles/faraday before the decomposition reaction has any effect.

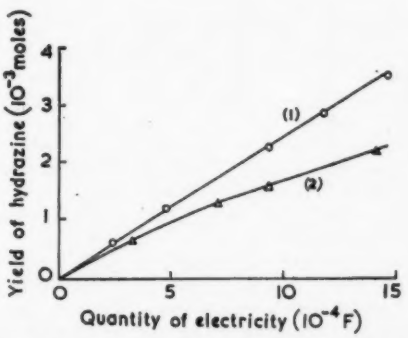


FIG. 2. Influence of current and quantity of electricity on yield of hydrazine. (1) 0·025A; (2) 0·1A.

(*b*) Current. In Fig. 2 are shown the hydrazine yield curves for two series of experiments carried out at currents of 0·025 and 0·1 A, respectively. The initial differential yields are not very different, but for a definite quantity of electricity the integrated yield is less at the higher current. This is contrary to what might be expected if the hydrazine yield depended upon the electric power dissipated in the discharge since this is about four times that at the lower current. Since it has been found that the c.d. in the glow spot falls with increase in current, it appears that the hydrazine yield is favoured by a high c.d.

(*c*) Stirring. In the normal arrangement of the cell hydrogen gas was evolved at the immersed cathode and produced considerable stirring in the solution near the glow spot. To ascertain whether this was beneficial the effect was tried of surrounding the cathode by a sheet of polyvinyl chloride which directed the gas to the side of the cell. Some of the results are listed in Table 1. Stirring has little effect upon the initial production of hydrazine, but increases it slightly as the hydrazine concentration increases.

TABLE 1.

Effect of stirring.

| Duration of electrolysis (min.) | Quantity of electricity ($10^{-4}$F) | Yield of hydrazine ($10^{-3}$ mole) | |
|---|---|---|---|
| | | Unstirred | Stirred |
| 15 | 2·33 | 0·55 | 0·61 |
| 30 | 4·65 | 1·23 | 1·21 |
| 60 | 9·30 | 2·38 | 2·27 |
| 120 | 18·6 | 4·27 | 4·32 |
| 240 | 37·2 | 7·25 | 8·0 |

*Influence of factors affecting the discharge.* (*a*) Electrode distance. Table 2 lists the yields of hydrazine obtained in experiments in which the distance of the anode from the liquid surface was varied from 0 to 1·1 cm.; each electrolysis was carried out under otherwise standard

conditions for 60 min. so that $9{\cdot}3 \times 10^{-4}$ F of electricity was passed. Except at small separations where the physical characteristics of the discharge change, the yield is almost independent of the anode–liquid separation.

(*b*) Pressure. Experiments were carried out under the above conditions, but with the standard distance of 0·5 cm. and with different pressures; the results are summarised in Table 3.

TABLE 2.

Effect of electrode distance.

| Anode–surface distance (cm.) ..... | 1·1 | 0·5 | 0·3 | 0·2 | 0·15 | 0 |
|---|---|---|---|---|---|---|
| Yield of hydrazine ($10^{-3}$ mole) ... | 2·27 | 2·27 | 2·05 | 1·94 | 1·80 | 1·58 |

TABLE 3.

Effect of pressure.

| Pressure (mm.) ..... | 70 | 85 | 100 | 148 | 175 |
|---|---|---|---|---|---|
| Yield of hydrazine ($10^{-3}$ mole) ..... | 2·13 | 2·19 | 2·27 | 2·15 | 2·20 |

The yield is practically independent of gas pressure.

*Influence of factors affecting the solution.* (*a*) Temperature. Variation of temperature is limited by the freezing point of the solution on the one hand and by the boiling of the ammonia on the other. Under the usual conditions a solid carbon dioxide cooling bath at −78·5° was used and during an hour's electrolysis the temperature of the electrolyte rose to −75°. By raising the working pressure to 150 mm. it was possible to electrolyse with a chloroform-containing bath at −63·5°, the temperature of the electrolyte rising during the experiment to −59°. The yields obtained in the two experiments were 2·25 and $2{\cdot}37 \times 10^{-3}$ mole of hydrazine, respectively. Thus a rise of temperature of about 15° brings about a small increase in the hydrazine yield.

(*b*) Nature of electrolyte and its concentration. It is not easy to find suitable inert electrolytes which are reasonably soluble in liquid ammonia, but Table 4 summarises the results obtained with various salts at different concentrations in 60 min. electrolyses under otherwise standard conditions. It is clear that the formation of hydrazine is not critically dependent

TABLE 4.

Influence of electrolyte.

| Electrolyte (M) | | Yield of hydrazine ($10^{-3}$ mole) | Electrolyte (M) | | Yield of hydrazine ($10^{-3}$ mole) |
|---|---|---|---|---|---|
| $NH_4NO_3$ ..... | 0·005 | 2·39 | $CH_3{\cdot}CO_2NH_4$ ... | 0·01 | 2·31 |
| | 0·01 | 2·27 | $KNO_3$ ..... | 0·01 | 2·07 |
| | 0·025 | 2·09 | $NH_4SCN$ ..... | 0·1 | 1·60 |
| | 0·05 | 1·95 | $NH_4NO_3$–$KNO_3$ | 0·01–0·09 | 1·82 |
| | 0·075 | 1·69 | $NH_4NO_3$–$KNO_3$ | 0·01–Satd. | 1·45 |
| | 0·1 | 1·59 | | | |

upon the nature or concentration of the electrolyte, but in general the highest yields are obtained in very dilute solution. Potassium nitrate seems less favourable than ammonium salts, and this may be connected with the formation of an electron solution at the cathode which exerts a scavenging action on radical precursors of the hydrazine.

(*c*) Poisons and catalysts. The effect of coating the cell walls with paraffin wax was investigated, and also in different experiments the cathode was platinised and poisoned by electrodepositing arsenic on it. None of these treatments affected the yield of hydrazine appreciably, indicating that it is not produced by a wall reaction and that the cathode is not involved in its production or decomposition.

*The Stationary Concentration of Hydrazine.*—The graph showing the variation of yield of hydrazine with quantity of electricity passed (Fig. 2) indicates that the differential yield decreases as the hydrazine accumulates in the electrolyte. To explore this further, experiments were carried out with solutions to which known amounts of pure hydrazine had been added; these were electrolysed for short times and the change in the amount of hydrazine with quantity of electricity passed was measured. The results are shown in Fig. 3 by plotting $d(N_2H_4)/dF$ against average hydrazine concentration. The graph is a shallow curve which cuts

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the axis at a hydrazine concentration of 2·04M, and this is the limiting stationary concentration which can be reached by glow-discharge electrolysis. Check experiments showed that this value was independent of the volume of the electrolyte and the gas pressure; it was raised slightly by increase of temperature.

*Analysis of Gaseous Products and the Material Balance.*—In order to examine the gaseous products formed, the apparatus was modified by decreasing the dead space and connecting the cell through a cold trap to a Sprengel pump and a gas-measuring and -sampling system. A considerable volume of gas was obtained which on analysis was found to contain only nitrogen and hydrogen, the latter being in excess of the amount to be expected from the complete dissociation of ammonia. On subtracting the volume of hydrogen corresponding to the hydrazine formed in the solution, the ratio $H_2 : N_2$ in the remaining gas was found to be 3·06 which indicates that a satisfactory material balance of nitrogen, hydrogen, and hydrazine exists. The volume of the gas obtained suggested that about 3 molecules of ammonia decompose into nitrogen and hydrogen for each molecule decomposing to give hydrazine under

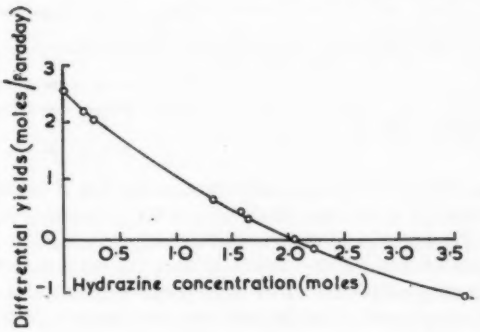


FIG. 3. Influence of hydrazine concentration on differential yield.

the particular conditions adopted. However, the decomposition of ammonia into nitrogen and hydrogen appeared to arise mainly from the electric discharge in the gas phase since similar amounts could be produced by passing a discharge between two metal electrodes in the ammonia vapour. No hydrazine could be detected under these conditions, however, indicating that the hydrazine arises exclusively in the present work by reaction in the liquid phase.

*Glow-discharge Electrolysis with Alternating Current.*—By supplying high voltage a.c. to the electrolytic cell it was possible to carry out glow-discharge electrolysis with alternating current; in these circumstances much heat is dissipated at the metal electrode in the gas phase, and the thin wire normally used had to be replaced by a massive platinum electrode. Except at low currents, where some rectification took place, the discharge struck in each half cycle so that the electrode in the gas phase was alternately anodic and cathodic. Hydrazine formation occurred in the liquid in the usual way, but the initial yield was only 1·32 moles/faraday. This is only slightly greater than half the normal yield and it suggests that the major portion of the hydrazine is formed when the gas phase electrode is anodic and the solution surface cathodic. This was confirmed by carrying out a d.c. glow-discharge electrolysis with the gas-phase electrode as a cathode; hydrazine was formed but in relatively small amount. This result is to be expected since it is only when the liquid surface is cathodic that a considerable fall of potential occurs at its surface

*Conventional Electrolysis of Liquid Ammonia Solutions.*—In the conventional electrolysis of liquid ammonia solutions with immersed electrodes it might be expected that $NH_2^-$ ions would discharge at the anode and that hydrazine might be formed to some extent, and this has in fact been claimed.[4] To clarify the position, electrolyses have been carried out with platinum, nickel, gold, and carbon anodes in ammonium nitrate solutions in liquid ammonia of various concentrations from 0·01 to 1·0M, and with a saturated solution of potassium amide, with c.d.'s varying from 0·05 to 1·0 A/sq. cm. In no case was hydrazine detected in the solution, and it seems that it does not arise in conventional electrolysis at all.

[4] Gessler and Pleskov, *J. Phys. Chem. U.S.S.R.*, 1950, **24**, 445.

## Discussion

The experimental results indicate clearly that the hydrazine is produced in the liquid and that the yield is closely related to the quantity of electricity passed; it is largely independent of other variables and in particular of the electric power dissipated in the discharge in the gaseous phase. The results are closely analogous to what has been observed [1] with aqueous systems and they agree with the view that the reaction is brought about by positive gaseous ions accelerated in the cathode fall and driven into the liquid. These might be expected to bring about reaction both by charge- and energy-transfer and since the yield of hydrazine is much greater than 1 equivalent/faraday it is apparent that the latter process is of importance.

Mass-spectrometer experiments suggest [5] that the main species present in ionised ammonia at low pressures are $NH_3^+$ and $NH_2^+$. The former reacts with ammonia to yield amino-radicals [6]

$$NH_3^+ + NH_3 \longrightarrow NH_4^+ + NH_2^\bullet \quad \ldots\ldots\ldots \text{(a)}$$

while the latter may react to give either amino-radicals

$$\left.\begin{aligned} NH_2^+ + NH_3 &\longrightarrow NH_2^+ + NH_2^\bullet \\ NH_2^+ + NH_3 &\longrightarrow NH_4^+ + NH_2^\bullet \end{aligned}\right\} \quad \ldots\ldots\ldots \text{(b)}$$

or imino-radicals

$$NH_2^+ + NH_3 \longrightarrow NH_4^+ + {}^\bullet NH^\bullet \quad \ldots\ldots\ldots \text{(c)}$$

Reaction (c) is energetically favourable but it involves considerable bond rearrangement, so that (b) is the most likely fate of $NH_2^+$ entering the liquid.

The energies of the gaseous ions on entering the liquid are not accurately known. The upper limit would be 390 ev if they passed through the cathode fall without undergoing retarding collisions. If it were possible to calculate the mean free path of the ions under the experimental conditions a precise estimate could probably be made [7] although experimental measurements [8] in gas discharges have suggested that the energies are probably greater than those expected for acceleration through one mean free path. The cathode fall in the present case is only slightly less than that in aqueous systems where an average energy of about 100 ev seems to fit the experimental results and thus it may be tentatively assumed that in the ammonia system the energies of the gaseous ions are of this order of magnitude. This is amply sufficient to bring about dissociation of ammonia molecules, either homolytically or *via* ionisation, since the energies required are

$$NH_3 \longrightarrow NH_2^\bullet + H^\bullet \quad \ldots\ldots 110 \text{ kcal./mole} \quad \text{(d)}$$
$$NH_3 \longrightarrow {}^\bullet NH^\bullet + 2H^\bullet \quad \ldots\ldots 153 \quad \text{,,} \quad \text{(e)}$$
$$NH_3 \longrightarrow {}^\bullet NH^\bullet + H_2 \quad \ldots\ldots 50 \quad \text{,,} \quad \text{(f)}$$

Reaction (f) is the most favourable reaction energetically, but it seems doubtful whether the formation of the hydrogen molecule could occur readily on spatial grounds; and, if this is so, (d) would be the preferred reaction.

Thus it seems likely that both charge-transfer and energy-transfer reactions will give amino-radicals as primary products, although the formation of imino-radicals cannot be completely excluded. Hydrazine might then be expected to arise by a dimerisation process

$$NH_2^\bullet + NH_2^\bullet \longrightarrow N_2H_4 \quad \ldots\ldots\ldots \text{(g)}$$

although the recombination reaction

$$NH_2^\bullet + H^\bullet \longrightarrow NH_3 \quad \ldots\ldots\ldots \text{(h)}$$

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[5] Mann, Hustrulid, and Tate, *Phys. Rev.*, 1940, **58**, 346.
[6] Dorfman and Noble, *J. Phys. Chem.*, 1959, **63**, 980.
[7] Compton and Morse, *Phys. Rev.*, 1927, **30**, 305.
[8] Choudrhi and Oliphant, *Proc. Roy. Soc.*, 1933, *A*, **87**, 662.

will be a possible competitor. Hydrogen atoms may also be removed by combination to give molecules

$$H\cdot + H\cdot \longrightarrow H_2 \quad \ldots\ldots\ldots\ldots \text{(i)}$$

The glow-discharge results suggest that hydrazine when it builds up to a sufficient concentration is decomposed by the very species which leads to its formation, and in photochemical and gas-discharge studies the reaction

$$NH_2\cdot + N_2H_4 \longrightarrow N_2H_3\cdot + NH_3 \quad \ldots\ldots\ldots\ldots \text{(j)}$$

has often been postulated. This may then be followed by further decomposition such as

$$\left.\begin{array}{l} N_2H_3\cdot + NH_2\cdot \longrightarrow N_2 + H_2 + NH_3 \\ \text{or} \quad 2N_2H_3\cdot \longrightarrow N_2 + 2NH_3 \end{array}\right\} \quad \ldots\ldots\ldots\ldots \text{(k)}$$

Thus the primary reactions in glow-discharge electrolysis of liquid ammonia are probably (a), (b), and (d) leading to $NH_2$ radicals as the precursors of the hydrazine subsequently formed. In this connection it is noteworthy that in some experiments on the glow-discharge electrolysis of liquid ammonia containing benzoic acid as a solute aminobenzoic acids could be detected among the products and the *o*-, *m*-, and *p*-aminobenzoic acid were separately recognisable by paper chromatography. After the primary act the immediate interaction of the active products is probably largely governed by spatial considerations, but once these species have diffused sufficiently far apart it seems likely that the reactions may be treated as homogeneous chemical reactions and that it is their competition which determines the yield of ultimate products obtained. Therefore it is proposed that the yield of $NH_2$ radicals/faraday remains constant throughout the electrolysis in the standard case, and that it is the velocity of the secondary reactions (g), (h), and (j) that governs the variation of the differential yield with hydrazine concentration. Thus if $n$ equivalents of $NH_2\cdot$ are formed per faraday, and if $v_1$, $v_2$, and $v_3$ are the velocities of reactions (h), (g), and (j) in the stationary state, then the differential hydrazine yield, $G$, in moles/faraday * at any time in the electrolysis will be given by

$$G = \frac{n}{2}\,\frac{(v_2 - v_3)}{v_1 + v_2 + v_3}. \quad (1)$$

If the velocities are expressed in terms of the concentrations of the reacting species this becomes

$$G = \frac{n}{2}\,\frac{k_2[NH_2]^2 - k_3[NH_2][N_2H_4]}{k_1[H][NH_2] + k_2[NH_2]^2 + k_3[NH_2][N_2H_4]}, \quad (2)$$

which simplifies to

$$G = \frac{n}{2}\,\frac{\frac{k_2}{k_3}[NH_2] - [N_2H_4]}{\frac{k_1}{k_3}[H] + \frac{k_2}{k_3}[NH_2] + [N_2H_4]}. \quad (3)$$

If it is assumed as an approximation that under a given set of experimental conditions the stationary concentrations of $NH_2$ radicals and hydrogen atoms are substantially constant, this may be written

$$G = \frac{n}{2}\,\frac{A - [N_2H_4]}{A + B + [N_2H_4]} \quad (4)$$

where $A = k_2[NH_2]/k_3$ and $B = k_1[H]/k_3$. This equation indicates that at the start of

* $G$, as used here, is not the same as that employed in radiation chemistry where the yield is expressed in molecules/100 ev. If, however, the average energy of the positively charged gaseous ions initiating the reactions were 100 ev it would be identical.

electrolysis the differential yield will be given by $G_0 = nA/2(A + B)$. It will decrease as the hydrazine concentration increases and becomes zero when $[N_2H_4] = A$. Furthermore, if $[N_2H_3]$ exceeds $A$ initially, then on glow-discharge electrolysis $G$ will be negative and the concentration of hydrazine will decrease until the stationary concentration is reached. This is qualitatively what is found in practice.

The various parameters may be elucidated from the experimental results as follows. $A$ is found directly from the stationary concentration of hydrazine. $B$ and $n$ may be calculated by taking experimental values of $G$ at different hydrazine concentrations and setting up a system of simultaneous equations. When this was done for the standard case, $A$ was found to be **2·04** and the average values of $n$ and $B$ were **12·5** and **2·96**, respectively. Thus the differential yield should be approximately given by

$$G = 6{\cdot}25\,\frac{2 - N_2H_4}{5 + N_2H_4}. \qquad (5)$$

This relation has been tested by calculating $G$ for different hydrazine concentrations and in Table 5 these calculated values are compared with those found experimentally.

TABLE 5.

Experimental and calculated hydrazine yields.

| $[N_2H_4]$ (M) | 0·2 | 0·4 | 0·6 | 0·8 | 1·0 | 1·2 | 1·4 | 1·6 | 1·8 | 2·0 | 2·2 |
|---|---|---|---|---|---|---|---|---|---|---|---|
| $G$, expt. | 2·19 | 1·88 | 1·61 | 1·35 | 1·09 | 0·85 | 0·62 | 0·41 | 0·22 | 0·04 | −0·14 |
| $G$, calcd. | 2·21 | 1·90 | 1·61 | 1·34 | 1·08 | 0·85 | 0·63 | 0·42 | 0·22 | 0·04 | −0·14 |

The agreement is very good, and while not too much importance should be attached to this since the method of calculating the parameters automatically ensures that certain experimental and calculated figures coincide, it does indicate that the form of the equation is correct. Equation (4) can be integrated to give the concentration of hydrazine which will exist after the passage of a quantity of electricity, $Q$ faradays, starting with no hydrazine initially present. The integrated equation is

$$\frac{nQ}{2V} = (2A + B)\log_e \frac{A}{A - [N_2H_4]} - [N_2H_4] \qquad (6)$$

where $V$ is the volume of the solution; and this equation also fits the experimental results satisfactorily.

The quantitative treatment given above, although it seems fairly successful, is certainly oversimplified. Thus in the conventional radiation chemistry of liquids it seems clear that the initial juxtaposition of radicals causes a proportion of them to combine regardless of competing reactions, and it is probable therefore that in the present case there is a molecular yield of hydrazine arising from the primary act which forms part of the total yield. Furthermore, local concentrations in the reaction zone are not necessarily the same as in the bulk liquid. In a more sophisticated treatment some allowance for these factors would have to be attempted, but as a first, rather crude approximation the present treatment seems adequate.

The influence of the main factors—quantity of electricity and hydrazine concentration—on the hydrazine yield can thus be reasonably interpreted on the mechanism proposed. Some light on the influence of secondary factors can be shed by considering the likely effect of c.d. in the reaction zone. It seems likely that the stationary radical and atom concentrations will be proportional to c.d. and, if this is so, the parameters $A$ and $B$ will be proportional also. It is then clear that the initial differential hydrazine yield, $G_0 = nA/2(A + B)$, will be independent of c.d., but the yield at a definite hydrazine

concentration (equation 4) will be higher the greater the c.d. This is qualitatively in agreement with what has been found for the variation of current; however, c.d. increases with rise of gas pressure but the effect on the hydrazine yield is slight.

The glow-discharge electrolysis of liquid ammonia has many features similar to those observed in aqueous systems.[1] Thus the product hydrazine is analogous to hydrogen peroxide which is formed in aqueous solutions when no oxidisable substrate is present, and the cathode fall of 390 v is similar to that of 415 v observed with water and occurs over practically the same distance. Moreover, the main phenomena can be accounted for by similar reaction schemes. The average $n$ value for ammonia of 12·5 is, however, substantially higher than that of 7·7 for water, although in view of the smaller dissociation energy of the H–$NH_2$ bond than of the H–OH bond a change in this direction is to be expected.

There is usually a striking parallelism between the results of glow-discharge electrolysis and the effect of ionising radiations, and in fact the gaseous ions postulated in the present work should be analogous in their action to a very intense beam of very low-energy α-particles. Until recently, little work had been reported on the radiolysis of liquid ammonia, but Dorfman [9] has now shown that electron radiolysis leads to substantial conversion into hydrazine, and Collinson, Cleaver, and Dainton [10] have made a very thorough and comprehensive study of the effect of $X$- and γ-radiolysis. They have shown that considerable hydrazine is produced and subsequently undergoes decomposition as its concentration increases in the liquid, and by using radical scavengers they have established that the $NH_2$ radical is involved in both processes. Thus as regards qualitative results and mechanism there is a striking measure of agreement between the two systems, but when the yield per unit of energy is considered the glow-discharge electrolysis appears to be a more efficient process for hydrazine production. Thus, if all the $NH_2$ radicals form hydrazine in the radiolysis the maximum yield appears to be about 1 mole per 100 ev, while the actual yield in glow-discharge can be as high as 2·5. The difference probably originates in the very different dose rates employed. In the radiolysis work the dose rate was of the order $5 \times 10^{18}$ ev $l.^{-1}$ $sec.^{-1}$. In the glow-discharge the dose rate is about $2 \times 10^{19}$ ev $l.^{-1}$ $sec.^{-1}$ and this is confined to a minute volume of solution immediately below the glow spot; the gaseous ions are unlikely to penetrate very far into the liquid and the volume might well be of the order of $10^{-5}$ ml., which would correspond to a dose rate per l. of about $10^{27}$ ev $sec.^{-1}$.

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Department of Inorganic and Physical Chemistry,
The University, Liverpool. [*Received, May 15th*, 1961.]

[9] Dorfman, A 1021, 17th International Congress for Pure and Applied Chemistry, 1960.
[10] Cleaver, Collinson, and Dainton, *Trans. Faraday Soc.*, 1960, **56**, 1640.

## 1025. *Glow-discharge Electrolysis. Part V.*[1] *The Contact Glow-discharge Electrolysis of Liquid Ammonia.*

By A. Hickling and G. R. Newns.

If liquid-ammonia solutions are electrolysed with a small thin wire anode immersed in them, then when the electric power dissipated is sufficiently great the anode becomes sheathed in vapour through which current passes by a type of glow-discharge. The chemical effects of this contact glow-discharge electrolysis have been investigated; hydrazine is the main product formed in solution, and the dependence of the yield on experimental variables has been studied. Electrolysis of ammonia–water mixtures by this technique also yields hydrazine in substantial amount provided less than 50% of water is present; increase in water content beyond this point causes the yield to decrease rapidly.

When the glow-discharge electrolysis of liquid ammonia described in Part IV [1] was being investigated, an experiment was performed in which the anode touched the surface of the electrolyte, and even so at a sufficiently high current density (c.d.) the liquid ammonia parted from the electrode and a glow-discharge was started and maintained. This result was investigated further by using thin platinum wire anodes immersed to a few centimetres' depth and a remarkable behaviour was observed. At first, on passage of a small current, conventional electrolysis took place with evolution of gas bubbles at the anode, and Ohm's law was obeyed with a relatively small cell voltage set up. However, when a sufficiently large current was passed the electrolysis became noisy with very vigorous gas evolution and a turbulent movement of the solution round the electrode, and the resistance increased. On still further increase in electric power a critical value was reached where a sharp change occurred; the potential across the cell increased to about 500 v and the current fell to about one-fifth of its former value, this change being accompanied by the formation of a greenish glow on the anode which appeared to extend a short distance into the solution through a vapour film which surrounded the electrode. In this last region hydrazine was formed in the solution, and this phenomenon of a luminous discharge at a high voltage at an anode immersed in a conducting solution is for convenience termed "contact glow-discharge electrolysis." It provides a very simple means of carrying out glow-discharge electrolysis, even at atmospheric pressure, and its investigation is described below.

### Experimental

The same vacuum apparatus, cell, and gas-sampling system were used as previously described.[1] The electrical circuit was simplified since the discharge was started merely by rapidly increasing the applied voltage from the power supply so that the induction coil and ballast resistances could be dispensed with. The cathode was the same as before but the anode was a thin platinum wire (0·025 cm. diameter) which was immersed in 40 ml. of liquid ammonia so as to have 0·1 sq. cm. of metal in contact with the solution. The wire was kept vertical and was part of a much longer piece which was suspended above the solution. This was found by trial to be the most successful arrangement for the anode, and methods where the anode was sealed into glass failed because during electrolysis the wire tended to melt at the point where it emerged from the glass.

The general technique was to add a weighed amount of ammonium nitrate as electrolyte to the cell and to dissolve it in 40 ml. of liquid ammonia. The electrodes were inserted and the applied voltage increased until the critical point was passed. The voltage was then readjusted to give the desired current. After the required quantity of electricity had been passed as indicated by a gas coulometer, the electrolysis was stopped and the cell contents were analysed as previously described. The standard experimental conditions adopted were:

[1] Part IV, preceding paper.

electrolyte, 40 ml. of 0·01M-solution of ammonium nitrate in liquid ammonia; pressure, atmospheric; anode, 0·1 sq. cm. of Pt wire, diameter 0·025 cm.; temperature, *ca.* −75°; current, 0·1 A.

## Results

*Physical Characteristics of the Discharge.*—In Fig. 1 A and B are shown the voltage–current graphs for the system at −75° at different pressures, and for different temperatures at 1 atm. pressure. They consist in general of three regions: at low voltages the current is linearly

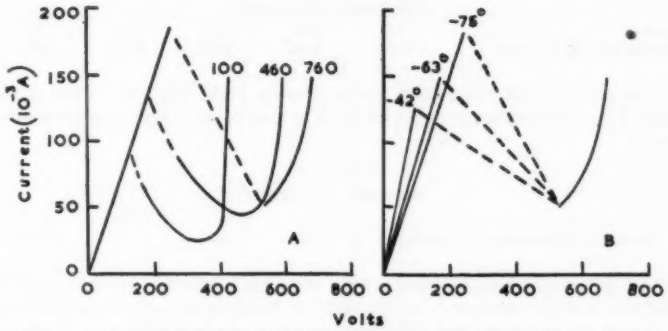


Fig. 1. Current-voltage graphs (A) at different pressures (mm.) at −75°, and (B) at different temperatures at 1 atm. pressure.

proportional to the applied voltage as expected; at voltages of more than 150 v there is an unstable region where current decreases while voltage rises; finally a stable region is entered where the anode is covered by the glowing discharge and the voltage is about 500 v. The general form of the voltage–current relation was independent of pressure and temperature, but the critical condition was most easily established at low pressures and high temperatures, and the final voltage was greater at higher pressures. In this glow-discharge region a limited variation of current was possible. The current had to be kept above about 0·07 A for the glow-

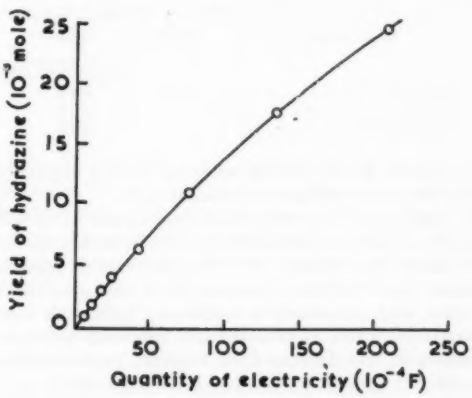


Fig. 2. Influence of quantity of electricity on yield of hydrazine.

discharge to be maintained, while above about 0·15 A the heat dissipated locally was sufficient to melt the electrode.

*Chemical Effects of Contact Glow-discharge.*—Hydrazine was produced under the glow-discharge conditions and in Fig. 2 is shown the yield plotted against quantity of electricity passed for the standard experimental conditions. The curve is very similar to that found for glow-discharge electrolysis with the vapour-phase anode [1] but the actual yield is smaller.

Thus in the present case the initial yield of hydrazine is about 1·8 moles/faraday as against 2·5 moles/faraday with the vapour-phase anode.

*Influence of Experimental Variables.—Pressure.* The yield of hydrazine was almost independent of the pressure as shown by the results in Table 1 for a series of electrolyses of 28½ min. duration over the pressure range 0·1—2 atm.; the quantity of electricity passed in each experiment was $17 \times 10^{-4}$ faraday and other conditions were standard.

TABLE 1.

Influence of pressure.

| Pressure (mm.) | 100 | 300 | 336 | 550 | 755 | 1520 |
|---|---|---|---|---|---|---|
| Yield of hydrazine ($10^{-3}$ mole) | 3·05 | 3·35 | 3·32 | 3·30 | 3·07 | 2·82 |

*Current.* Increase of current raised the hydrazine yield slightly. This is shown by the results in Table 2 for currents in the range 0·07—0·15 A under standard conditions with $17 \times 10^{-4}$ faraday passed.

TABLE 2.

Influence of current.

| Current (A) | 0·07 | 0·10 | 0·15 |
|---|---|---|---|
| Yield of hydrazine ($10^{-3}$ mole) | 2·23 | 3·07 | 3·13 |

*Temperature.* The yield of hydrazine was not much affected by temperature, although there was perhaps a slight tendency for the yield to decrease at higher temperatures, as shown in Table 3; standard conditions and the same quantity of electricity were again used.

TABLE 3.

Influence of temperature.

| Temperature | −75° | −46° | −33·5° |
|---|---|---|---|
| Yield of hydrazine ($10^{-3}$ mole) | 3·07 | 2·85 | 2·90 |

*Electrolyte concentration.* Table 4 shows the yield obtained with several electrolytes at different concentrations under standard conditions with the usual quantity of electricity.

TABLE 4.

Effect of electrolyte concentration.

| Electrolyte | 0·005 | 0·01 | 0·1 | 0·4 | 1·0M |
|---|---|---|---|---|---|
| | Yield of hydrazine ($10^{-3}$ mole) | | | | |
| $NH_4NO_3$ | 2·78 | 3·07 | 3·75 | — | 4·26 |
| $KNO_3$ | — | 2·29 | 2·65 | 2·97 | — |
| $CH_3{\cdot}CO_2NH_4$ | — | 2·65 | 2·91 | — | — |

In contrast to the results obtained with a vapour-phase anode,[1] the yield increases appreciably with rise of electrolyte concentration.

*The Stationary Concentration of Hydrazine.*—The differential hydrazine yield under standard conditions at various hydrazine concentrations was determined as described previously,[1] and Fig. 3 shows the results. As with the vapour-phase anode, the yield drops with increasing hydrazine concentration, showing that the glow-discharge can initiate a decomposition of hydrazine, and ultimately a stationary hydrazine concentration is achieved. This occurred at about 1·0M which is substantially less than with the vapour-phase anode.[1] The stationary concentration was decreased by increase in electrolyte concentration, and slightly by rise of temperature; pressure seemed to have little effect.

*Analysis of Gaseous Products and the Material Balance.*—The gas evolved contained only nitrogen and hydrogen, the latter being in excess of the amount to be expected from the complete dissociation of ammonia. When the hydrogen equivalent to the hydrazine formed was allowed for, a material balance was achieved within the limits of experimental error. As in the previous investigation,[1] considerable decomposition of ammonia other than that leading to hydrazine seems to occur, and the results indicated that only about one-quarter of the total ammonia decomposed was involved in the hydrazine producing reaction.

*Glow-discharge Electrolysis of Ammonia–Water Mixtures.*—The contact glow-discharge electrolysis of a complete range of water–ammonia mixtures was studied under standard conditions, and some experiments with the mixtures containing most water were also made at 0°; the usual quantity of electricity was passed. The mixtures were made either by distilling appropriate quantities of ammonia into aqueous ammonia (*d* 0·880) in the cell, the latter being cooled meanwhile by liquid nitrogen, or for mixtures containing less than 35% of ammonia the aqueous ammonia was diluted with water. After electrolysis the solutions were evaporated and neutralised, or simply neutralised where the ammonia was present in small amount, and analysed for hydrazine, hydrogen peroxide, and hydroxylamine. Only in the electrolysis of aqueous solutions containing no ammonia was hydrogen peroxide detected, and

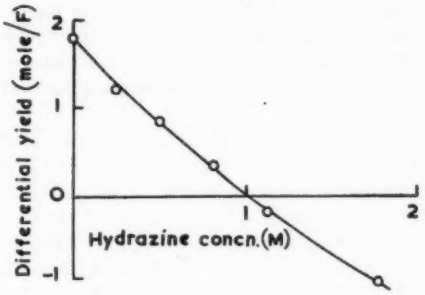


FIG. 3. Influence of hydrazine concentration on differential yield.

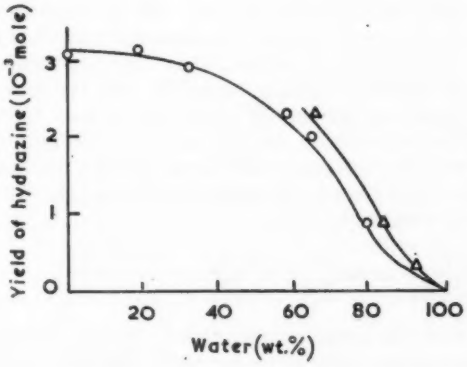


FIG. 4. Hydrazine yields in ammonia–water mixtures.
○, −75°. △, 0°.

in no experiment could a reaction for hydroxylamine be found. Hydrazine was formed in yields dependent on the ammonia content, as shown in Fig. 4. The yield of hydrazine remained almost constant with increase in water content until the solution contained more than 50% of water. Increase in water beyond this point caused the yield to decrease rapidly, and it was zero, of course, for 100% water. In the region of low ammonia content, increase in temperature to 0° resulted in an increase in hydrazine yield.

## DISCUSSION

It has been shown that the transition from conventional to contact glow-discharge electrolysis at a wire anode occurs abruptly as the voltage is increased, and the transition occurs at lower power dissipation if the pressure is decreased or the temperature of the solution is raised. This relates the ease of transition to the readiness of vaporisation of the solvent and suggests that in contact glow-discharge local heating at the electrode must produce a sheath of solvent vapour through which conduction takes place. Kellogg,[2] in seeking to imitate the anode effect found in molten electrolytes, showed that a similar phenomenon

[2] Kellogg, *J. Electrochem. Soc.*, 1950, **97**, 133.

could be produced in aqueous solutions when the surface of the electrode reached the boiling point of water, although he did not use sufficiently high voltages for full glow-discharge to be established. Thus the present phenomenon may well be one of general occurrence in any conducting liquid under appropriate conditions although the detailed mechanism of the effect obviously needs further study. It is noteworthy that once contact glow-discharge is set up it is self-maintaining; if the vapour sheath should collapse for any reason and the liquid touch the electrode, then there is a surge in current and power dissipated bringing about further vaporisation. The electrode is undoubtedly hot under glow-discharge conditions, and a small increase in current serves to make it visibly red-hot.

Contact glow-discharge electrolysis could also be carried out with alternating instead of direct current, and with direct current making the electrode a cathode, but the working conditions were then much more critical since much of the energy dissipated in the discharge occurred at the metal surface instead of in the liquid, and the thin wires tended to melt readily.

In comparing the results of contact glow-discharge electrolysis with those where a vapour-phase anode at reduced pressure is used, the marked differences in the form of the discharge must be borne in mind. In contact glow-discharge the thickness of the vapour envelope is not known but it is probably much less than 1 mm. and it may well depend on experimental conditions. Thus the cathode fall of potential, which is of paramount importance, may differ from that observed with the vapour-phase anode where the discharge usually takes place over a much greater distance. Further, instead of a glow-spot of self-regulating area, in contact glow-discharge the area will be determined by the surface of the vapour sheath, and the c.d. may thus be very different from that in the glow-spot. When these differences are considered it is remarkable how very similar are the chemical effects of the two types of discharge in liquid ammonia, and this leaves little doubt that the chemical reactions occurring are similar in the two cases. If the same mechanism is adopted for contact glow-discharge, *i.e.*, the production of $NH_2$ radicals which undergo various competing reactions, then the results can be quantitatively interpreted as in the previous paper.[1] The treatment leads to an expression for the differential yield of hydrazine ($G$ expressed in moles/faraday) as follows:

$$G = \frac{n}{2} \cdot \frac{A - [N_2H_4]}{A + B + [N_2H_4]} = 6{\cdot}0\,\frac{1{\cdot}0 - [N_2H_4]}{3{\cdot}4 + [N_2H_4]},$$

and this equation is in good agreement with the experimental results. The equation is closely similar to that found for the vapour-phase anode, and $n$ has nearly the same value, but $A$ and $B$ are appreciably different. The difference implies that in contact glow-discharge electrolysis the stationary concentrations of $NH_2$ radicals and hydrogen atoms in the reaction zone are less than when the vapour-phase anode is used.

The variation of hydrazine yield with composition in ammonia–water mixtures is at first sight unexpected. However, if it is taken that there are three main species present in the mixtures, *viz.*, $NH_3$, $NH_3,H_2O$ or $NH_4OH$, and $H_2O$ molecules, and that $NH_3$ and $NH_3,H_2O$ are equivalent in producing $NH_2$ radicals on collision with the initiating gaseous ions while the $H_2O$ molecules simply function as diluents, then the explanation of the results is immediately apparent. The differential yield of hydrazine in a particular mixture should be given by

$$G_{\text{mixture}} = \frac{[NH_3] + [NH_3,H_2O]}{[NH_3] + [NH_3,H_2O] + [H_2O]}\,G_{\text{ammonia}}$$

Ignoring in the first instance the dissociation of the hydrate, the amount of water present would have to exceed 51% before free water molecules began to reduce the hydrazine yield substantially. In practice the position is complicated by the dissociation of the

$NH_3,H_2O$, and this will lead to a small decrease in the hydrazine yield as the amount of water increases, followed by a much more rapid decrease as the amount of water exceeds the stoicheiometric value for the hydrate.

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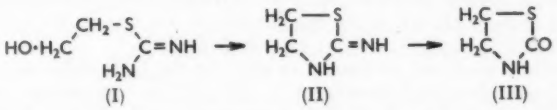
## 1026. *Some Derivatives of* S-(2-*Hydroxyethyl*)*thiourea.*

By L. A. CORT.

The hydrobromide of *S*-(2-hydroxyethyl)thiourea decomposes above its melting point to yield 1,4-dithian, as do also the hydrobromides of the *O*-formyl and the *O*-acetyl derivative. The picrate can be titrated with alkali hydroxides. Attempted preparation of the hydriodide of the *O*-formyl compound led to tetrathiourea hydriodide.

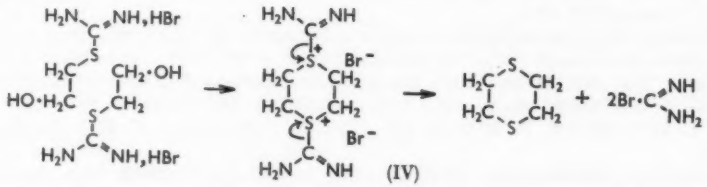
THE melting behaviour [1] of the picrate of *S*-(2-hydroxyethyl)thiourea (I) suggests that ring-closure might be occurring to give the picrate of 2-iminothiazolidine (II) (or of the tautomer, 2-amino-2-thiazoline). However, the action of heat on the picrate, on the one gram scale, did not lead to the known thiazolidine picrate; only ammonium picrate



(I) (II) (III)

was isolated. It is possible that the water produced in the condensation (I) ⟶ (II) effects hydrolysis to give thiazolid-2-one (III) and ammonia, but since it did not appear practicable to increase the scale of the experiment attention was directed to other salts.

The hydrobromide of *S*-(2-hydroxyethyl)thiourea (I) behaved like the picrate in that after melting it re-solidified as the temperature was raised. However, in this case there is clearly no scheme of reaction (I) ⟶ (II) ⟶ (III); no 2-iminothiazolidine, thiazolid-2-one, or derivative thereof could be isolated; instead the products were 1,4-dithian and polymeric material.



(IV)

It is likely that the first step in this reaction is dimerisation to give a diquaternary salt (IV), and that this then undergoes dissociation. It would be expected that the bromoformamidine formed would rearrange to cyanamide hydrobromide, which would polymerise to dicyanamide and melamine, as is known [2] to be the case with chloroformamidine.

After removal of the 1,4-dithian, the residue was largely soluble in both hot dilute acid

[1] Cort and Pearson, *J.*, 1960, 1686.
[2] Johnson and Sprague, *J. Amer. Chem. Soc.*, 1939, **61**, 176; Mulder and Smit, *Ber.*, 1874, **7**, 1634.

and alkali, but no derivatives of 2-mercaptoethylamine could be isolated from these solutions (cf. acid hydrolysis [3] of thiazolines), confirming that there has been no condensation (I) ⟶ (II).

The hydrobromide *S*-(2-formyloxyethyl)thiourea and that of the *O*-acetate also decomposed above the melting point, and both gave 1,4-dithian, but in very much lower yield.

On treatment with dilute aqueous sodium hydroxide and benzoyl chloride, *S*-(2-hydroxyethyl)thiourea hydrobromide yielded benzoylthioethyl benzoate (as would be expected), but when sodium hydrogen carbonate was used in place of the hydroxide, the tribenzoyl derivative of the free base was obtained.

The picrate of the thiourea (I) could be titrated with 0·1N-sodium hydroxide, to give the molecular weight within ±3%; this is expected to be capable of useful extension.

In one experiment, for the attempted preparation of the hydriodide of *S*-(2-formyloxyethyl)thiourea, a product was isolated which analysed satisfactorily for tetrathiourea hydriodide. This is the first reported case of a compound of this type with acids, such compounds usually having the formula $(H_2N{\cdot}CS{\cdot}NH_2)_2HX$, although tetrathiourea complexes are known with salts.

## Experimental

M. p.s are corrected.

S-(2-*Hydroxyethyl*)*thiouronium Bromide*.—Prepared in the usual manner (in acetone) from ethylene bromohydrin, the bromide (77%) crystallised after 72 hr. It had m. p. 73—80° and was hygroscopic (some preparations were deliquescent; Olin and Dains [4] record the salt as an oil). Treatment with benzoyl chloride and 2N-sodium hydroxide gave the dibenzoyl derivative (m. p. 39°; prisms from methanol) of 2-mercaptoethanol (lit.,[5] m. p. 39°) (Found: C, 67·1; H, 4·6; S, 11·5. Calc. for $C_{16}H_{14}O_3S$: C, 67·1; H, 4·9; S, 11·2%).

Use of 0·1N-sodium hydrogen carbonate in place of the hydroxide led to the isolation of NN′-*dibenzoyl*-S-(2-*benzoyloxyethyl*)*thiourea*, m. p. 156°, needles from acetone–methanol (Found: C, 67·7; H, 4·75; N, 6·6; S, 7·4. $C_{24}H_{20}N_2O_4S$ requires C, 66·7; H, 4·6; N, 6·5; S, 7·4%).

It did not prove possible to isolate a salt from the hydrobromide, with trichloroacetic, benzoic, or 3,5-dinitrobenzoic acids, but the picrate [1] was readily obtained.

*Titration of the Picrate*.—Titration with 0·1N-sodium hydroxide was possible provided that attention was paid to the following points: aqueous acetone (1 : 2) was a suitable solvent; ethyl bis-2,4-dinitrophenylacetate was a suitable indicator (as used similarly [6] with picrates of hydrocarbons); it was necessary to add the alkali dropwise throughout, never to let it accumulate in local excess, and never to add further alkali when some previously added remained unneutralised. Titration to the stable end-point was a slow procedure, up to 5 hr. for 0·8 g. of picrate, but results were usefully reproducible (Found: *M*, 359, 353, 349, 341, 347. $C_9H_{11}N_5O_8S$ requires *M*, 349).

S-(2-*Formyloxyethyl*)*thiouronium Bromide*.—Prepared (in acetone) from 2-bromoethyl formate, the crude bromide (84%) was hygroscopic (m. p. 90—95°). It failed to yield a picrate in methanol, but after several days the solution deposited *S*-(2-hydroxyethyl)thiouronium picrate, m. p. and mixed m. p. 154—158°, re-solidifies 162°, re-melts 239—243° (decomp.) (Found: C, 31·2; H, 2·9; N, 20·0; S, 8·9. Calc. for $C_9H_{11}N_5O_8S$: C, 31·0; H, 3·2; N, 20·1; S, 9·2%).

S-(2-*Acetoxyethyl*)*thiouronium Bromide*.—The hygroscopic bromide was obtained (62%) from 2-bromoethyl acetate. Crystallisation from acetone–light petroleum (b. p. 60—80°) gave needles, m. p. 92—95° (lit.,[4] m. p. 99°) (Found: C, 24·7; H, 4·3; Br, 32·8; N, 11·3; S, 13·3. Calc. for $C_5H_{11}BrN_2O_2S$: C, 24·7; H, 4·6; Br, 32·9; N, 11·6; S, 13·2%). This salt behaved, as regards picrate formation, like the *O*-formyl compound.

*Action of Heat on the Salts*.—(*a*) *S*-(2-Hydroxyethyl)thiouronium picrate (1·0 g.) was heated from 150° to 180° during 8 min., then held at 180° for 3 min. After melting it slowly resolidified

[3] Crawhall and Elliott, *J.*, 1952, 3094; 1951, 2071.
[4] Olin and Dains, *J. Amer. Chem. Soc.*, 1930, **52**, 3322.
[5] Fromm and Jörg, *Ber.*, 1925, **58**, 306.
[6] "Organic Reagents for Organic Analysis," Hopkin and Williams, Ltd., 2nd edn., 1950, p. 112.

(with considerable effervescence at 170°). Crystallisation from aqueous acetone gave deep yellow prisms (0·3 g.), m. p. 258—275° (decomp.) (ammonium picrate?), which liberated ammonia with cold 0·1N-sodium hydroxide. (The picrates of 2-amino-2-thiazoline and 2-mercaptoethylamine have m. p. 235° and 126°, respectively.[7,8])

(*b*) *S*-(2-Hydroxyethyl)thiouronium bromide (10 g.) was melted and heated to 170°; it re-solidified with effervescence at *ca.* 160°. Treatment of a methanol extract with picric acid gave ammonium picrate (1·1 g.), orange-red orthorhombic biprisms (from acetone–benzene), m. p. 287—290° (decomp.) (Found: C, 29·35; H, 2·6; N, 22·8. Calc. for $C_6H_6N_4O_7$: C, 29·3; H, 2·5; N, 22·8%). The residue from the methanol extract was almost completely insoluble in cold dilute acid and alkali.

The product from 15 g. of bromide was extracted with carbon disulphide, to give 1,4-dithian (0·8 g., 18%), hexagonal plates, m. p. 110—111° (from acetone) (lit.,[9] m. p. 111°) (Found: C, 40·0; H, 6·6; S, 53·4. Calc. for $C_4H_8S_2$: C, 40·0; H, 6·7; S, 53·3%). (Thiazolid-2-one [10] has m. p. 52°, from carbon disulphide.)

The product from 20 g. of bromide was boiled with 2N-potassium hydroxide in 80% ethanol (300 ml.); some material (2·1 g.) did not dissolve during 1 hr. The action of benzoyl chloride on the filtrate yielded no solid derivative.

A similar hydrolysis by 3N-sulphuric acid also gave a solid residue (1·7 g.). Half of the filtrate yielded no solid derivative with benzoyl chloride and alkali; the other half with picric acid yielded yellow prisms (50 mg.) which did not melt below 360°, and did not liberate ammonia with alkali. No derivatives of 2-mercaptoethylamine (cf. ref. 8) were obtained. The solid residues were soluble in cold concentrated sulphuric acid; dilution produced amorphous material only.

(*c*) *S*-(2-Formyloxyethyl)thiouronium bromide (5 g.) gave a clear melt. Effervescence commenced at *ca.* 160°, and the material slowly (15 min.) solidified when held at 200°. Extraction by carbon disulphide gave 1,4-dithian (120 mg.), m. p. 104—107°, m. p. and mixed m. p. 111° after crystallisation from acetone. The residue was almost completely soluble in hot water (20 ml.); the solution yielded, with picric acid, only ammonium picrate [2·9 g.; m. p. and mixed m. p. 285—290° (decomp.)].

(*d*) With *S*-(2-acetoxyethyl)thiouronium bromide effervescence commenced in the molten bromide at *ca.* 150°. There was considerable darkening and the material appeared to have resolidified after 30 min. at 200°. Extraction by carbon disulphide gave 1,4-dithian (210 mg. from 20 g. of bromide), m. p. 100—107°, m. p. and mixed m. p. 111° after crystallisation.

*Attempted Preparation of* S-(2-*Formyloxyethyl*)*thiouronium Iodide.*—2-Chloroethyl formate (12·5 g.), sodium iodide (17·4 g.), and thiourea (12·1 g.) were boiled together in acetone (50 ml.) during 8 hr. After a further 12 hr. the deposited sodium chloride (8·7 g.) was removed and the solution set aside for 7 days. The crystals which separated (3·2 g.) had m. p. 170—180° (decomp.). Recrystallisation from acetone–benzene (poor recovery) furnished felted needles of *tetrathiourea hydriodide*, m. p. 193° [Found: C, 11·2; H, 4·3; I, 28·8; N, 26·3; S, 29·35. $(H_2N{\cdot}CS{\cdot}NH_2)_4{,}HI$ requires C, 11·1; H, 4·0; I, 29·35; N, 25·9; S, 29·7%].

Attempts to obtain this compounds by saturating a solution of thiourea in acetone with hydrogen iodide were unsuccessful; thiourea was recovered (m. p. and mixed m. p. 179°).

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[*Received, May 26th,* 1961.]

[7] Schöberl, Kawohl, and Hamm, *Chem. Ber.*, 1951, **84**, 571.
[8] Gabriel and Colman, *Ber.*, 1912, **45**, 1643.
[9] Masson, *J.*, 1886, **49**, 234.
[10] Michels and Gever, *J. Amer. Chem. Soc.*, 1956, **78**, 5350.

XUM

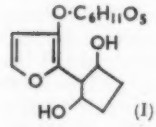
## 1027. *Aucubin.*

By A. J. Birch, J. Grimshaw, and H. R. Juneja.

Reduction of aucubin by lithium and ammonia gave a dideoxyaucubin (isolated as its tetra-acetate). The corresponding aglucone proved stable and its reactions confirm structure (V) proposed for aucubin by Japanese workers.[1] A preliminary account[2] of our work has been published. Swiss[3,4] workers have also published supporting evidence for structure (V).

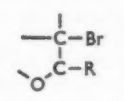
The glucoside of *Aucuba japonica*, Thunb., was first obtained pure by Bourquelot and Hérissey[5] who named it aucubin (aucuboside). Later workers[6] showed aucubin to be identical with rhinanthin isolated[7] in 1870 from the seeds of *Rhinanthus* species, but on the recommendation of Bridel and Braecke[6] the name aucubin has been retained for this glucoside as the original rhinanthin was not pure. Aucubin is of very wide occurrence in Nature[8] and is found in large quantities in individual plants. Seeds of *Melampyrum*[6] and of *Rhinanthus* species[7] have been known since classical times as the troublesome contaminants of wheat which cause the resulting bread to be black. This blackening is due to aucubin. Aucubin appears to be the active principle[9] of *Plantago* species, for many years recommended in the French Pharmacopœia as a general panacea. It increases the rate of removal of uric acid from the body,[10] and the aglucone has antibiotic activity.[11]

Bourquelot and Hérissey[5] showed aucubin to be a β-glucoside whose aglucone is very unstable and rapidly affords an insoluble black amorphous powder on treatment with acid. Little progress was made with structural investigation until Karrer and Schmid[12] prepared derivatives of the aglucone. They showed that aucubin has the molecular formula $C_{15}H_{22}O_9$, containing six hydroxyl groups, four of which are accounted for by the glucose moiety, and two double bonds and an inert oxygen atom. The remaining two oxygen atoms are accounted for by the glucopyranose ring and the glycosidic link. Catalytic hydrogenation of aucubin hexa-acetate gave a saturated tetrahydro-derivative. Acid treatment of tetrahydroaucubin afforded anhydrotetrahydroaucubigenin formulated as (IV) with one secondary hydroxyl group and two inert oxygen atoms. Karrer and



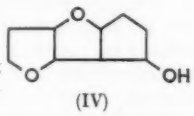

(I)

(II)




(III) a: R = OAlK

b: R = –N(CO·CH2 / CO·CH2)




(IV)

Schmid's structural proposal (I) for aucubin was influenced by an observation by Bergmann and Michalis[13] that one atom of bromine is substituted in aucubin hexa-acetate in methanol and by their own observation that lead tetra-acetate introduces a further acetoxy-group into aucubin hexa-acetate. Karrer and Schmid interpreted these reactions as indicating the presence in aucubin of a furan ring, but this is not in accord with the subsequent work of Clauson-Kaas and his collaborators on the reaction between furan

[1] Fujise, Obara, and Uda, *Chem. and Ind.*, 1960, 289; Fujise, Uda, Ishikawa, Obara, and Fujino, *ibid.*, 1959, 954.
[2] Grimshaw and Juneja, *Chem. and Ind.*, 1960, 656.
[3] Wendt, Haegele, Simonitsch, and Schmid, *Helv. Chim. Acta*, 1960, **43**, 1440.
[4] Haegele, Kaplan, and Schmid, *Tetrahedron Letters*, 1961, No. 3, 110.
[5] Bourquelot and Hérissey, *Compt. rend.*, 1902, **134**, 1441; 1904, **138**, 1114; *Ann. Chim. Phys.*, 1905, **4**, 289.
[6] Bridel and Braecke, *Compt. rend.*, 1922, **175**, 533; 640.
[7] Ludwig, *Arch. Pharm.*, 1870, **192**, 199; 1872, **199**, 6.
[8] Paris and Chaslot, *Ann. Pharm. franç.*, 1955, **13**, 648.
[9] Bourdier, *J. Pharm. Chim.*, 1907, **26**, 254.
[10] Kato, *Folia Pharmacol. Japonica*, 1946, **42**, 37 (*Chem. Abs.*, 1953, **47**, 1843).
[11] Rombouts and Links, *Experientia*, 1956, **12**, 78.
[12] Karrer and Schmid, *Helv. Chim. Acta*, 1946, **29**, 525.
[13] Bergmann and Michalis, *Ber.*, 1927, **60**, 935.

and bromine in methanol [14] to give the dihydro-diether (II; R = Me) and the action of lead tetra-acetate on furan [15] to give the corresponding diacetate (II; R = Ac). During the course of our work Japanese authors [1] proposed structure (V) for aucubin and confirmed the nature of the carbon skeleton by converting anhydrotetrahydroaucubigenin, now formulated as (VI), into the acid (VII) whose anhydride methyl ester showed an infrared spectrum identical with that of the synthetic racemate. Our work, briefly reported elsewhere,[2] provides alternative evidence for the nature and arrangement of the functional groups. Schmid and his collaborators [3,4] also published alternative evidence confirming this structure for aucubin and from nulcear magnetic resonance evidence [4] favour a *cis*-junction of the rings.

We first examined Bergmann and Michalis's " bromoaucubin hexa-acetate," m. p. 182°. This may be prepared from aucubin hexa-acetate by the action of bromine in methanol [13] or by using *N*-bromosuccinimide and crystallising the product from methanol.[12] Analysis revealed a methoxyl group (missed by previous workers). Methanol which was liberated by acid hydrolysis of this derivative was characterised as formaldehyde dimethone. A different bromo-compound was obtained on bromination of aucubin hexa-acetate in ethanol. Thus bromination in methanol results in the addition of the elements of methyl hypobromite across one double bond. This observation led us to suppose that aucubin contains an enol-ether ethylenic link and to seek an explanation of the " aromatic substitution " of aucubin on this basis.

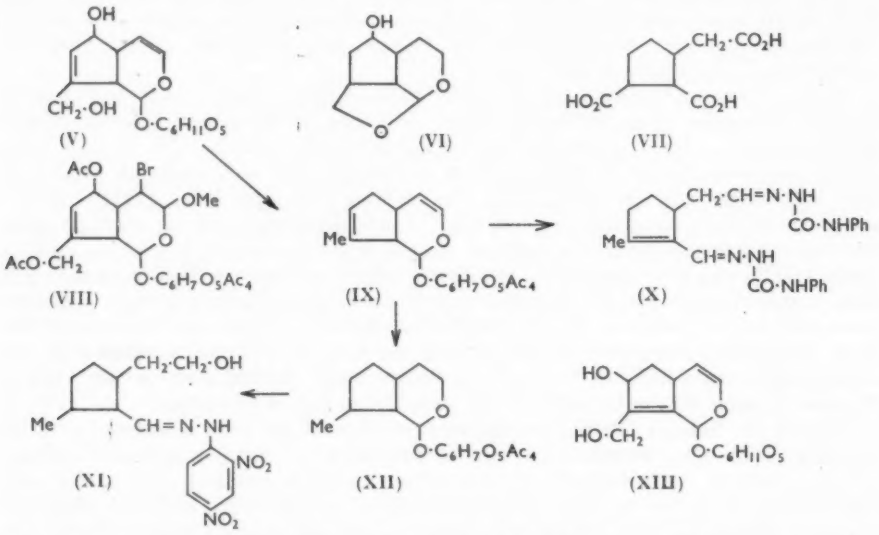
It is well known that enol ethers rapidly form addition products with two atoms of chlorine or bromine in an indifferent solvent and that the resulting α-halogeno-ether is easily converted into an α-alkoxy-ether by reaction with an alcohol.[16] Thus it seems readily acceptable that in alcoholic solution the final product of bromination of an enol-ether will be the ether bromide (IIIa), the aucubin derivative being (VIII). Such a reaction is shown by the glucoside plumieride [17] which also contains an enol-ether grouping. The enol-ether double bond also combines with *N*-bromosuccinimide to give the addition product (IIIb) which in refluxing alcohol affords [18] the ether bromide (IIIa) in an analogous manner to Karrer and Schmid's bromination procedure for aucubin hexa-acetate. Dihydropyran with lead tetra-acetate gives a substitution product,[19] as does aucubin hexa-acetate. With 2,3-dihydrofuran, however, this reagent reacts in an alternative manner to give 2,3-diacetoxytetrahydrofuran.[20] Thus one double bond and the inert oxygen atom of the aucubin aglucone can be satisfactorily placed in an enol-ether system.

Part of the difficulty in the investigation of aucubin has been associated with the instability of the aglucone and this in turn must be due to the highly unsaturated carbonyl systems produced on hydrolysis. Evidence from the hydrogenation experiments mentioned above suggested that one hydroxyl group at least is allylic and accordingly the substance was treated with lithium and ethanol in ammonia in an attempt to remove some of the functional groups. The product, $C_{15}H_{22}O_7$, of this reaction is a dideoxyaucubin, isolated as its tetra-acetyl derivative, $C_{15}H_{18}O_7Ac_4$ (IX). Alkaline hydrolysis followed by acid treatment gave glucose and a comparatively stable, steam-volatile, water-soluble aglucone, dideoxyaucubigenin. Tetra-*O*-acetyldideoxyaucubin formed a methyl ether bromide and absorbed two mol. of hydrogen on catalytic hydrogenation; it therefore contains two double bonds, one in the intact enol-ether grouping. Two different tetrahydro-derivatives were obtained when hydrogenation was carried out in mildly acid solution, but only one of them was obtained in neutral solution; they are presumably stereoisomers (XII).

[14] Clauson-Kaas, Limborg, and Fakstorp, *Acta Chem. Scand.*, 1948, **2**, 109.
[15] Clauson-Kaas and Elming, *Acta Chem. Scand.*, 1952, **6**, 535; Elming, *ibid.*, p. 578.
[16] Wislicenus, *Annalen*, 1878, **192**, 111; Riobé, *Bull. Soc. chim. France*, 1951, 829.
[17] Halpern and Schmid, *Helv. Chim. Acta*, 1958, **41**, 1109.
[18] Paul and Tchelitcheff, *Compt. rend.*, 1953, **236**, 1968.
[19] Hurd and Edwards, *J. Org. Chem.*, 1954, **19**, 1319.
[20] Normant, *Compt. rend.*, 1949, **228**, 102.

The dideoxyaucubigenin was characterised as the bisphenylsemicarbazone (X) of an optically active dicarbonyl compound, $C_9H_{12}O_2$. Kuhn–Roth oxidation of this derivative indicated the presence of one *C*-Me group, in contrast to aucubin which contains none. The ultraviolet absorption of the phenylsemicarbazone, $\lambda_{max.}$ 248 and 286 mμ, corresponds to the presence of derivatives of an isolated and an αβ-unsaturated carbonyl group.[21] Acid hydrolysis of tetra-*O*-acetyldideoxytetrahydroaucubin, m. p. 91°, gave a steam-volatile aglucone characterised as the 2,4-dinitrophenylhydrazone (XI) of a monocarbonyl compound, $C_9H_{16}O_2$.

These results are reconcilable with the presence in aucubin of (*a*) an allylic [22] primary hydroxyl group which gives rise to the new *C*-Me group and which must also be involved in forming the second ethereal oxygen group of anhydrotetrahydroaucubigenin (VI); (*b*) a further allylic hydroxyl group which must become the secondary hydroxyl function of anhydrotetrahydroaucubigenin where it is present in a five-membered ring since the corresponding ketone shows $\nu_{max.}$ 1747 cm.$^{-1}$; (*c*) the system C=C·O·C·O·C$_6$H$_{11}$O$_5$ as part of a ring. The last system on hydrolysis gives rise to the two carbonyl groups detectable in dideoxyaucubigenin and the one carbonyl group detectable in the hydrogenated compound




the latter group arising from the acetal system. The *C*-Me group of dideoxyaucubin is unlikely to be attached to the system (*c*) since on the one hand the corresponding aglucone does not give the iodoform reaction and on the other hexa-*O*-acetylaucubin methyl ether bromide is inert [13] towards nucleophilic substitution. A band in the infrared spectrum of aucubin at 1655 cm.$^{-1}$ can be attributed to the enol-ether group.[23] It is present in the spectra of hexa-*O*-acetylaucubin and tetra-*O*-acetyldideoxyaucubin, but is absent from the spectra of the bromo-methyl ethers and tetrahydro-derivatives. Neither aucubin nor tetra-*O*-acetyldideoxyaucubin shows selective ultraviolet absorption corresponding to conjugated double bonds: the system C=C·C=C·O in particular must be absent. The αβ-unsaturated carbonyl chromophore in the dideoxyaucubigenin derivative must be produced therefore by conjugation of one double bond with the carbonyl group formed by hydrolysis of the acetal. This acetal-oxygen is unlikely to be in an allyl ether position

[21] Grammaticakis, *Bull. Soc. chim. France*, 1949, 410.
[22] Birch, *Quart. Rev.*, 1950, **4**, 71.
[23] Davison and Bates, *J.*, 1953, 2607; Meakins, *J.*, 1953, 4170.

since hydrogenolysis should then have occurred with ease during reduction with lithium in ammonia.

All this evidence can be accommodated by the formula (V) proposed for aucubin by the Japanese workers. In particular, chemical evidence is presented for the unusual type of heterocyclic ring. We had deduced formula (V) as being the most likely for aucubin as the ease with which anhydrotetrahydroaucubigenin (VI) is formed in acid solution severely restricts structural possibilities. We rejected structure (XIII) suggested by Schmid,[3] though later withdrawn,[4] since this formula contains an allylic acetal group.

## Experimental

M. p.s were taken on a Kofler block standardised against substances of known m. p. Light petroleum of b. p. 60—80° was used. Ultraviolet spectra were measured for absolute ethanol solutions.

*Isolation of Aucubin.*—Trim and Hill's procedure [14] was used. *Aucuba japonica* leaves collected from shrubs growing in Heaton Mersey, Stockport, at intervals from June to October afforded 1—2% of their fresh weight as aucubin. Aucubin hydrate crystallised from 90% alcohol as colourless needles, m. p. 180—181°, showing no selective absorption in the ultraviolet region at wavelengths longer than 215 mμ, and a band in the infrared region at 1655 cm.$^{-1}$ (Nujol mull). Aucubin hexa-acetate, needles, m. p. 128° (from aqueous methanol), showed infrared bands at 1755 and 1655 cm.$^{-1}$ (in $CCl_4$).

*Hexa-O-acetyl-4-bromo-3,4-dihydro-3-methoxyaucubin* (VIII).—Prepared according to the procedure of Bergmann and Michalis,[13] this *compound*, crystallised from ethyl acetate–light petroleum as colourless needles, m. p. 181—182° (lit.,[13] m. p. 182°) (Found: Br, 11·6; OMe, 4·6. $C_{23}H_{37}BrO_{16}$ requires Br, 11·3; OMe, 4·4%), $\nu_{max.}$ 1747 cm.$^{-1}$ (in Nujol mull). A sample (0·3 g.) was refluxed with N-sulphuric acid (25 ml.) for 30 min., then about half of the solvent was distilled off. This distillate was redistilled from sodium carbonate and the second distillate again distilled from a little sodium dichromate and sulphuric acid. The final distillate gave formaldehyde dimethone, m. p. and mixed m. p. 189°.

Hexa-*O*-acetylaucubin (0·2 g.), dissolved in ethanol (20 ml.), was cooled to 0° and bromine (0·057 g.) in ethanol (6 ml.) slowly added. After 2 hr., water was added and the precipitate collected. The analogous *ethyl ether* crystallised from ethyl acetate–light petroleum as needles, m. p. 117—118° (with resolidification and m. p. 159—160°) (Found: C, 48·0; H, 5·4; Br, 11·25. $C_{29}H_{39}BrO_{16}$ requires C, 48·1; H, 5·4; Br, 11·1%).

*Anhydrotetrahydroaucubigenin* (VI). Aucubin was hydrogenated and the products were treated with dilute hydrochloric acid as described by Karrer and Schmid.[12] The product was isolated by continuous ether extraction followed by chromatography of the extract, in chloroform, over alkaline alumina (Peter Spence's grade H). Elution with chloroform afforded, after removal of the solvent, anhydrotetrahydroaucubigenin, needles (from ether), m. p. 89—90° (lit.,[12] m. p. 90·5°), in yields similar to those previously reported. The corresponding ketone showed an infrared band at 1747 cm.$^{-1}$ (in $CCl_4$).

*Dideoxyaucubin Tetra-acetate* (IX).—Lithium (1 g.) was added in 2 hr. with stirring to aucubin hydrate (1 g.) in liquid ammonia (200 ml.) and ethanol (6 ml.). After an excess of lithium had remained for 1 hr. this was destroyed by addition of ammonium sulphate. Ethanol and water were then added and the ammonia allowed to evaporate, then the solution was saturated with carbon dioxide and evaporated to dryness. The residue was extracted with hot methanol. Evaporation of the methanol solution left a gum which was left overnight in pyridine (6 ml.) and acetic anhydride (4 ml.). Addition of water precipitated crystals which after several recrystallisations from methanol afforded *dideoxyaucubin tetra-acetate* as needles (0·45 g.), m. p. 137—138°, $[\alpha]_D^{22}$ −142° (*c* 0·5 in $CHCl_3$) (Found: C, 57·3; H, 6·3; Ac, 31·3. $C_{23}H_{30}O_{11}$ requires C, 57·4; H, 6·2; 4Ac, 35·8%), slowly becoming yellow in air. The compound showed no selective ultraviolet absorption at $\lambda > 215$ mμ, and infrared bands at 1760, 1744, and 1665 cm.$^{-1}$ (in Nujol mull). The free glucoside was a gum.

*Bromination of Dideoxyaucubin Tetra-acetate.*—The above acetate (0·1 g.), dissolved in methanol (10 ml.), was cooled to 0° and bromine (0·034 g.) in methanol (3·4 ml.) slowly added. Addition of water precipitated the *bromo-methoxy-adduct* which crystallised from light petroleum

[14] Trim and Hill, *Biochem. J.*, 1952, **50**, 310.

as needles, m. p. 124—126° (decomp.) (Found: C, 48·8; H, 5·8; Br, 14·0; OMe, 5·7. $C_{24}H_{33}BrO_{12}$ requires C, 48·6; H, 5·6; Br, 13·5; OMe, 5·2%).

*Tetrahydrodideoxyaucubin Tetra-acetate* (XII).—Dideoxyaucubin tetra-acetate (0·15 g.) in ethyl acetate containing a trace of acetic acid was hydrogenated over Adams catalyst (30 mg.) at room temperature and pressure (uptake 21·4 ml. at N.T.P.; $2H_2 = 20·0$ ml.; 20 min.). Catalyst and solvent were removed and the residue fractionally crystallised from aqueous methanol to give a less soluble *tetrahydro-derivative* as laths (0·02 g.), m. p. 141—142°, $[\alpha]_D^{23}$ +240° (*c* 0·3 in MeOH) (Found: C, 56·7; H, 7·1. $C_{23}H_{34}O_{11}$ requires C, 56·7; H, 7·0%), and a more soluble *tetrahydro-derivative* as square plates (0·08 g.), m. p. 90—91°, $[\alpha]_D^{23}$ +97° (*c* 0·5 in MeOH) (Found: C, 57·0; H, 6·95%). When hydrogenation was carried out with rigorous exclusion of acid then only the derivative of m. p. 91° was obtained.

*Dideoxyaucubigenin Bisphenylsemicarbazone* (X).—Dideoxyaucubigenin tetra-acetate (0·17 g.) was refluxed for 30 min. under nitrogen with N-sodium hydroxide (10 ml.), then 2N-sulphuric acid (10 ml.) was added. After 1 hour's refluxing under nitrogen the clear solution was steam-distilled until the distillate no longer gave an instantaneous precipitate with Brady's reagent. This distillate, $\lambda_{max.}$ 259 mμ, did not give the iodoform test and afforded the *bisphenylsemicarbazone*, needles (from ethanol), m. p. 203—204° (decomp.), $[\alpha]_D^{25}$ +128° (*c* 0·4 in $CHCl_3$) (Found: C, 66·2; H, 6·2; N, 20·0; *C*-Me, 3·8. $C_{23}H_{26}N_6O_2$ requires C, 66·1; H, 6·2; N, 20·3; 1*C*-Me, 3·6%), $\lambda_{max.}$ 248 (log ε 4·5) and 286 mμ (log ε 4·5). The residual solution from steam-distillation was neutralised with sodium carbonate and evaporated to dryness. Extraction of the residue with methanol gave a gum which yielded β-glucose penta-acetate, m. p. and mixed m. p. 134—135°.

*Tetrahydrodideoxyaucubigenin 2,4-Dinitrophenylhydrazone* (XI).—Tetrahydrodideoxyaucubin tetra-acetate, m. p. 91° (50 mg.), was refluxed under nitrogen with N-sodium hydroxide (5 ml.) for 30 min., then tartaric acid (2 g.) in water was added and the mixture steam-distilled. From the distillate 2,4-dinitrophenylhydrazine in dilute hydrochloric acid slowly precipitated 2,4-dinitrophenylhydrazone which was collected after 12 hr. Crystallisation from aqueous ethanol afforded orange needles, m. p. 129—132° (Found: C, 52·9; H, 5·9; N, 16·1. Calc. for $C_{15}H_{20}N_4O_5$: C, 53·4; H, 5·9; N, 16·5%). This is probably the stereoisomer obtained by the Japanese authors [1] who give m. p. 134—136°.

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## 1028. *Counter-ion Fixation in Alginates.*

By A. KATCHALSKY, R. E. COOPER, J. UPADHYAY, and A. WASSERMANN.

Donnan equilibria between alginate sols or highly swollen gels and uni- or bi-valent counter-ions were measured and from the results the fractions, $\phi_p$, of the free counter-ions and the mean activity coefficients of the free ions in the sols or gels were calculated. For comparison counter-ion fixation was also studied by an osmotic method. Both series of measurements showed that the $\phi_p$ values of the bivalent or complexing counter-ions are relatively small. The relevance for previously described mechanochemical effects is discussed.

IT is known that some negatively charged macromolecules are capable of binding simple cations (see refs. 1—3 and earlier literature cited there). In order to increase the

[1] Mock and Marshall, *J. Polymer Sci.*, 1954, **13**, 263; Kagawa and Katsuura, *ibid.*, 1955, **17**, 365; Nagasawa and Kagawa, *ibid.*, 1957, **25**, 61; Nagasawa, Izumi, and Kagawa, *ibid.*, 1959, **37**, 375; **38**, 213.

[2] Alexandrowicz, *J. Polymer Sci.*, 1960, **43**, 325, 337.

[3] Katchalsky, Alexandrowicz, and Kedem, "Polyelectrolyte Solutions," Interscience Publ. Inc., New York, in preparation.

XUM

knowledge of these effects the cation fixation by alginates * has now been investigated. This work is also of interest for an understanding of the mechanochemistry of swollen cylindrical alginate gels,[5] and of molecular size and shape changes accompanying the conversion of sodium or potassium into magnesium alginate.[6]

This paper deals with alginic acid gels and with alginates fully neutralised by one type of counter-ions, no attempt being made to deal with systems containing different cations. The binding of sodium, potassium, ammonium, hydrogen, silver, ethylenediammonium, magnesium, calcium, and cupric ions has been deduced from a study of Donnan and osmotic equilibria. The former technique is applicable to sols and gels and enables, moreover, a computation to be made of the activity coefficients of the permeant electrolyte in presence of the alginates. Attempts to deduce counterion fixation from Donnan equilibria have been made before (see, *e.g.*, ref. 7), but the present method of calculation has not been used hitherto.

*Theoretical.*—Recent investigations [2] have shown that the osmotic pressure, $\pi$, of a solution containing a uni-univalent salt and a polyelectrolyte can be expressed by $\pi = \pi_p + \pi_s$, where $\pi_p$ is the osmotic pressure of the polyelectrolyte solution without the salt and $\pi_s$ is the osmotic pressure of the salt solution free from macromolecules; $\pi_p$ is given by $(RT/1000)(m_p + m_p\nu\phi_p)$, where $m_p$ is the molarity of the polyelectrolyte, $\nu$ is the number of charges per macromolecule, and $\phi_p$ is the osmotically active fraction of the counter-ions. In most systems here considered $\nu$ equals $P$, the total number of carboxylate groups in the fully neutralised alginic acid, so that $m_p\nu$ equals $m_pP$ or $m_m$, the last symbol indicating the concentrations of repeating unit in moles per litre. The product $\nu\phi_p$ can be taken as the effective charge on the macromolecule and $m_p\nu\phi_p$, which equals $m_m\phi_p$, is the concentration of " free " counter-ions. Experiment [1,2] and theory [3] show that $\phi_p$ is determined by the charge density on the polyelectrolyte rather than by its concentration or the ionic strength of the solution, and it appears that each macromolecule contributes $\phi_p$ free counter-ions whatever the contribution of permeant electrolytes in the solution.

In this situation one is justified [2,3] in expressing the activity of a uni-univalent salt in a polyelectrolyte solution by

$$a_s = (m_p\nu\phi_p + m_s)m_sf^2, \quad (1)$$

where $m_s$ is the concentration of the uni-univalent salt and $f$ is the mean activity coefficient of the " free " ions. As usual the activity is the product of the activities of counter- and co-ions, each activity being obtained by multiplying the concentration of the " free " ions with an activity coefficient, probably similar to that of the salt without the polyelectrolyte. If a Donnan equilibrium is set up, the equality of activities is represented by

$$(m_p\nu\phi_p + m_s)m_sf^2 = (m_s')^2f'^2. \quad (2)$$

Here and below primed symbols relate to permeant electrolytes free from macromolecules. In equations (2), (3), (4), and (8) a factor depending on solvent activities [8] has been omitted because it is close to unity in the systems here considered.

If an alginate anion with $P$ carboxylate groups is fully neutralised by a bivalent counter-ion $X^{2+}$, the resulting species, $Alg^{P-}X_{P/2}^{2+}$ may be in equilibrium with a permeant

* The repeating units of alginic acid are D-mannuronic and L-guluronic acid.[4] This polyelectrolyte is either a mixture of poly-D-mannuronic and poly-L-guluronic acid or a copolymer; in the latter case the copolymer composition may depend on the degree of polymerisation.

[4] Fischer and Doerfel, *Z. physiol. Chem.*, 1955, **302**, 186.
[5] Mongar and Wassermann, *J.*, 1952, 492, 500, 510; Harkness and Wassermann, *ibid.*, p. 497; MacArthur, Mongar, and Wassermann, *Nature*, 1949, **164**, 110.
[6] Buchner, Cooper, and Wassermann, *J.*, 1961, 3974.
[7] Strauss and Anders, *J. Amer. Chem. Soc.*, 1958, **80**, 6494.
[8] Donnan and Guggenheim, *Z. phys. Chem.*, 1932, *A*, **162**, 346.

bi-univalent salt, $X^{2+}Y_2^-$ or with a bi-bivalent salt, $X^{2+}Y^{2-}$. Considerations similar to those leading to equation (2) show that the Donnan equilibrium conditions are

$$(m_s + m_m\phi_p/2)4m_s^2f^3 = 4(m_s')^3f'^3, \quad (3)$$

$$(m_s + m_m\phi_p/2)m_sf^2 = (m_s')^2f'^2. \quad (4)$$

On rearrangement of expressions (2), (3), and (4) and replacement of $\nu m_p$ by $m_m$ one obtains (5), (6), and (7) which apply to uni-univalent, bi-univalent, and bi-bivalent salts, respectively.

$$m_s = [(m_s')^2/m_s][(f')^2/f^2] - \phi_p m_m, \quad (5)$$

$$m_s = [(m_s')^3/m_s^2][(f')^3/f^3] - \phi_p m_m/2, \quad (6)$$

$$m_s = [(m')^2/m_s][(f')^2/f^2] - \phi_p m_m/2. \quad (7)$$

So far it has been assumed that covalent-bond formation plays no significant rôle in the counter-ion fixation. In systems where this assumption is not justified, an equilibrium constant, $K$, has to be introduced. To show this we consider the equilibrium between alginic and hydrochloric acid and designate chloride-ion concentrations by $m_{Cl}$ and $m_{Cl}'$. Equality of activities of hydrochloric acid solutions with and without alginic acid requires that

$$(\alpha\phi_p m_m + m_{Cl})m_{Cl}f^2 = (m_{Cl}')^2(f')^2, \quad (8)$$

where $\alpha$, the degree of ionisation of alginic acid, equals $\nu m_p/m_m$. The mass-action law requires that

$$\alpha \times a_{H^+}/(1 - \alpha) = K, \quad (9)$$

$a_{H^+}$ being the activity of the hydrogen ions, which may be identified with the first terms, $\alpha\phi_p m_m$ and $m_{Cl}$, in expression (8). In presence of hydrochloric acid, $\alpha \ll 1$, so that

$$\alpha(\alpha\phi_p m_m + m_{Cl}) = K. \quad (10)$$

Dividing (10) by (8) and introducing the resulting expression for $\alpha$ in (10) lead to

$$(m_{Cl}')^2 = [(m_{Cl}')^4/m_{Cl}^2](f'^2/f^2) - K\phi_p m_m(f^2/f'^2). \quad (11)$$

If, therefore, the ratios of the activity coefficients, the $\phi_p$ values, and the product $K\phi_p$ in expressions (5), (6), (7), and (11) remain effectively constant, their numerical values can be computed from the slopes and intercepts of the straight line obtained by plotting $m_s$ against $(m_s')^2/m_s$ and $(m_s')^3/m_s^2$, or $m_{Cl}'^2$ against $(m_{Cl}')^4/m_{Cl}^2$. If it is possible to determine $K$ by an independent method, $\phi_p$ in expression (11) can also be estimated. Alternatively one can make the reasonable assumption that $\phi_p$ approaches unity if $\alpha \ll 1$; if this is accepted, equation (11) enables one to estimate $K$ from a study of Donnan equilibria.

## Experimental

Two commercial sodium alginate samples (A) and (B) were used. The weight-average molecular weights (in 0·100M-sodium chloride at 22—24°) were respectively $(1·5 \pm 0·3) \times 10^5$ and $(5·3 \pm 1·3) \times 10^4$. Alginic acid and potassium, magnesium, calcium, copper, and silver alginate were prepared from sample (A) by techniques described previously.[5,6] Ammonium and ethylenediammonium alginate were made from sample (B), which was first converted into alginic acid by treatment with N-hydrochloric acid; after being washed with water, the fully swollen alginic acid gel was neutralised with ammonia or ethylenediamine, the pH being controlled with the help of a glass electrode and a Cambridge Instrument Co. pH meter. All alginates were freed from permeant electrolytes by dialysis against water or 1 : 1 water–acetone, or by washing of the fully swollen gels with water. The complete removal of permeant electrolyte from sols used for osmotic tests was checked by electrical-conductance measurements. All alginates were analysed by methods already described[5,6] and it was found that the ratio, counter-ion : carboxylate (equiv.), was 1·00 ± 0·03. No attempt was made to estimate the

relative quantities of D-mannuronic and L-guluronic acid residues; a few measurements of optical rotation and rotary dispersion indicated that these ion-exchange reactions did not influence the stereochemical composition of the polyanion. (Earlier work [9] had shown that the specific optical rotation of sodium alginate is not significantly dependent on the molecular weight.) For a determination of the concentration $m_m$ in the fully swollen gels, their specific gravity had to be determined.

*Donnan Equilibria.*—Alginate sols were filled in Cellophane bags, which were placed in glass-stoppered tubes containing solutions of the permeant electrolytes. The tubes were shaken in a thermostat bath until equilibrium was reached. Tests were carried out in which the initial solution in the Cellophane bag contained the alginate together with the permeant electrolyte, while the initial liquid outside was water. It was thus established that the same equilibrium was reached from both sides. Control experiments were carried out in which the bags, without the sols, were shaken with water or with a solution of the permeant electrolytes. In some of the tests the bags had been washed with a solution of EDTA sodium salt. The fully swollen fibrous gels (fibre diameter 0·1—0·4 mm.) were stirred or shaken with the solutions of the permeant electrolyte until equilibrium was reached. The equilibrated solution was separated from the gel by low-speed centrifugation.[5] The centrifuged gels were extracted with water until all permeant electrolytes had been removed. Control experiments showed that the composition of the gels was unaffected by centrifugation. The concentrations of the permeant electrolytes were determined by standard analytical methods, with an accuracy of 0·2—0·3%. Alginate concentrations in sols or gels were measured [5,6] with an accuracy of ±5%; in most cases there was no significant change during establishment of the Donnan equilibrium. The experiments with sols were done at 25·0° and those with gels at 22—24°; separate tests showed that between 20° and 25° the equilibrium positions were not detectably altered. The results in the last four lines of Table 1 were calculated from data obtained by Mongar.[10]

*Osmotic-concentration Method.*—This has been described by Alexandrowicz,[11] whose technique was used without essential modifications. Two samples of polyethylene glycols (supplied severally by Petrochemicals and by Croda Ltd.) of weight-average molecular weight, $M_w$, 4800 ± 200 (sample I) and 7400 ± 300 (sample II) were used to afford the solutions of known activity. The light-scattering equipment used for the standardisation has been described.[12] Purification was by high-speed centrifugation followed by filtration through sintered glass (porosity No. 5). The concentration dependence of the osmotic coefficient, $\phi$, of the two polyethylene glycol samples was similar to that found by Alexandrowicz,[11] the $\phi$ values of sample (II) being larger. If, for instance, the glycol concentration was 1·00 g. per 100 ml. of solution, $\phi$ values of, respectively, 1·12 and 1·33 were observed. Tests were carried out in which the sodium ion fixation was determined with both standards: there was no significant difference. "Viskin" regenerated-cellulose membranes, which had been treated at 100° with a dilute solution of EDTA sodium salt, were used. To hasten attainment of equilibrium, the osmometers were shaken. In a typical experiment, a solution of sodium alginate (sample A) (0·133 g. per 100 ml.) was equilibrated against a solution of polyethylene glycol [sample (II)]; after 23, 30, and 46 hr. the interpolated glycol concentrations, corresponding to no solvent transport, were 1·00, 1·01, and 1·00 g. per 100 ml. of solution.

## Results

In studying the Donnan equilibria, experiments were carried out in which the concentration of the polyelectrolytes or of the permeant electrolyte was kept constant, the variables being respectively $m_s$, or $m_{Cl}$ and $m_m$. Plots of $m_s$ or $(m_{Cl}')^2$ against $(m_s')^2/m_s$, $(m_s')^3/m_s^2$, or $(m_{Cl}')^4/m_{Cl}^2$ were straight lines, within the limits of the experimental errors, as shown for typical cases in the Figures. Numerical values of the ratios * of the activity coefficients, $\phi_p$, and $\phi_p K$ (see equations 5, 6, 7, and 11) were then calculated and are given in Table 1. The $K$ value

* Those in columns 7 and 8 of Table 1 relate respectively to equations 5—7 and equation 11.

[9] Rose, Ph.D. Thesis, London, 1937, Table H; Vincent, Goring, and Young, *J. Appl. Chem.*, 1955, **5**, 374.

[10] Mongar, Ph.D. Thesis, London, 1951, Table 14 and unpublished results.

[11] Alexandrowicz, *J. Polymer Sci.*, 1959, **40**, 107, 113.

[12] French, Roubinek, and Wassermann, *J.*, 1961, 1953.

in the last line is of the same order of magnitude as that of alginic acid deduced from potentiometric titration [13] in aqueous suspension. In the case of silver alginate $\phi_p$ and $K$ were calculated from equations (5) and (11) which fit the observation equally well. It is not possible, therefore, to use these results in order to decide whether the binding of the silver ion is governed by a

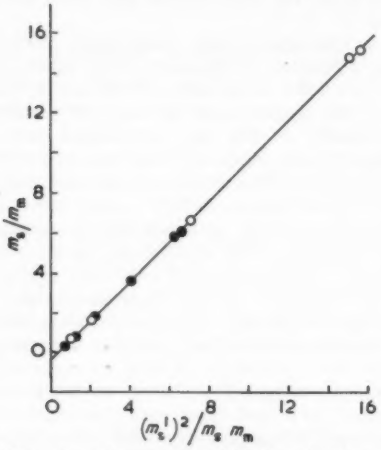


FIG. 1. Donnan equilibrium between sodium alginate sol and sodium chloride solution at 25·0°. Plot of $m_s/m_m$ against $(m_s')^2/(m_s m_m)$. The concentration $m_s'$ and $m_s$ are in moles l.$^{-1}$; $m_m$ in monomoles of alginate per l. of sol.

● $m_m = 0{\cdot}0165$. ○ $m_m = 0{\cdot}00650$.

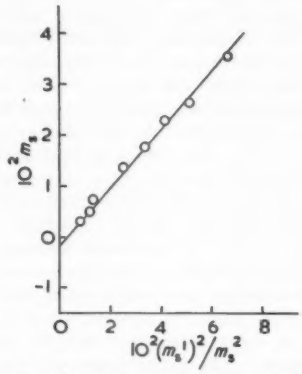


FIG. 2. Donnan equilibrium between fully swollen fibrous calcium alginate gel (fibre diameter 0·4 mm.) and calcium chloride solution at 23·5°. Plot of $m_s$ against $(m_s')^2/m_s^2$, concentration being in mole l.$^{-1}$; $m_m$ was 0·308 monomole of alginate per l. of fully swollen gel.

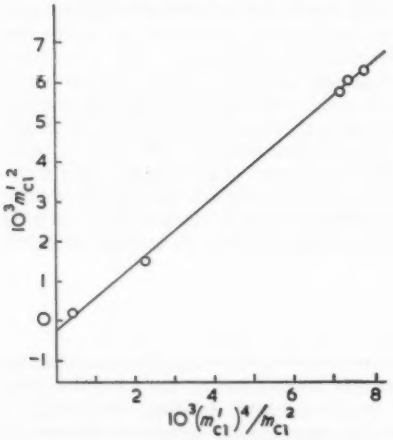


FIG. 3. Donnan and mass-action equilibrium between fully swollen fibrous alginic acid gels (fibre diameter 0·4 mm.) and hydrochloric acid solution at 22°. Plot of $(m_{Cl}')^2$ against $(m_{Cl}')^4/m_{Cl}^2$, concentrations being expressed in moles l.$^{-1}$; $m_m$ was 0·341 monomole of alginic acid per l. of fully swollen gel.

mass-action equilibrium. The activity coefficients, $f$, in the last column of Table 1 were computed from the slopes in columns 7 and 8, by using the activity coefficients $f'$ of column 11, taken from the literature [14] and relating to concentrations near the arithmetic mean of the values given in column 5. The difference between the concentrations of the "free" ions inside a sol or gel and in the external solution is not large in any of the systems here considered.

[13] McGee, Fowler, and Kenyon, *J. Amer. Chem. Soc.*, 1947, **69**, 353.

[14] Harned and Owen, "The Physical Chemistry of Electrolytic Solutions," 2nd ed., Reinhold Publ. Corp., New York, 1950.

It is understandable, therefore, why, for a given concentration, the $f$ and $f'$ values are similar. This is not incompatible with the slopes, deviating significantly from unity, if the ratios of the activity coefficients appear in the second or third power.

The $\phi_p$ values obtained with the help of the osmotic concentration method are in Table 2.

TABLE 1.

Counter-ion fixation in alginate sols and gels at 22—25°. Results of Donnan equilibrium measurements.

| Alginate sol. | Alginate gel. | P.E.* | Concentration range: Alginates (equiv./l.) | Concentration range: P.E.* (mole/l.) | No.† | $(f'/f)^{2 \text{ or } 3}$ | $(f'/f)^2$ | $\phi_p$ | $10^4K$ (mole/l.) | $f^1$ | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Na | | NaCl | 0·00658—0·0165 | 0·00518—0·103 | 11 | 1·0 ± 0·03 | | 0·40 ± 0·05 | | 0·86 ± 0·07 | 0·86 ± 0·10 |
| K | | KCl | 0·00600—0·0164 | 0·00641—0·100 | 8 | 1·0 ± 0·03 | | 0·35 ± 0·05 | | 0·92 ± 0·03 | 0·92 ± 0·06 |
| $NH_4$ | | $NH_4Cl$ | 0·0104 | 0·00200—0·0138 | 8 | 1·0 ± 0·05 | | 0·27 ± 0·05 | | 0·90 ± 0·03 | 0·90 ± 0·06 |
| Mg | | $MgCl_2$ | 0·00610—0·0167 | 0·00358—0·0303 | 17 | 1·00 ± 0·05 | | 0·15 ± 0·02 | | 0·60 ± 0·08 | 0·60 ± 0·1 |
| ED‡ | | ED‡ chloride | 0·00567—0·00602 | 0·00251—0·0219 | 13 | 0·97 ± 0·04 | | <0·02 | | | |
| | Ca | $CaCl_2$ | 0·308 | 0·00440—0·0432 | 8 | 0·55 ± 0·05 | | 0·01 ± 0·005 | | 0·70 ± 0·1 | 0·85 ± 0·1 |
| | Cu | $CuSO_4$ | 0·291 | 0·00430—0·0618 | 17 | 1·6 ± 0·2 | | 0·03 ± 0·02 | | 0·27 ± 0·05 | 0·21 ± 0·05 |
| | Ag | $AgNO_3$ | 0·218 | 0·00830—0·0874 | 8 | 0·80 ± 0·08 | 0·76 ± 0·08 | 0·03 ± 0·015 | 2 ± 1§ | >0·73 | >0·81 |
| | H | HCl | 0·341 | 0·00830—0·768¶ | 9 | | 0·86 ± 0·1 | | 8 ± 4§ | 0·91 ± 0·07 | 0·95 ± 0·05 |

* P.E. = Permeant electrolyte. ‡ ED = Ethylenediammonium.
† No. = Number of tests. § Calc. from equation 11, with $\phi_p = 1$.
¶ Fig. 3 represents results obtained with the lowest five concentrations in this range; the results obtained from tests with the highest four concentrations fall on a continuation of the straight line shown in the Figure.

TABLE 2.

Counter-ion fixation in alginate sols at 22—25°; results of osmotic measurements.

| Alginate | Conc. range (equiv. $l.^{-1}$) | No. of tests | $\phi_p$ |
|---|---|---|---|
| Na * | 0·00500—0·0136 | 7 | 0·29 ± 0·05 |
| Na † | 0·0115 | 1 | 0·33 ± 0·05 |
| K | 0·00460—0·0190 | 3 | 0·31 ± 0·05 |
| $NH_4$ | 0·00300—0·0100 | 3 | 0·30 ± 0·05 |
| Ethylenediammonium | 0·00474—0·0116 | 4 | 0·07 ± 0·01 |
| Mg | 0·00398—0·0136 | 5 | 0·16 ± 0·02 |

* Weight-average molecular weight, $M_w = 1·5 \times 10^5$. † $M_w = 5·3 \times 10^4$.

## DISCUSSION

Ion fixation by the three non-complex-forming univalent counter-ions, sodium, potassium, and ammonium is similar, as shown by the $\phi_p$ values in the first three lines of Table 1 and in the first four lines of Table 2. These values show that 60—70% of the counter-ions are sequestered by the polyanion. Similar binding of univalent counter-ions was found for other polycarboxylic acids.[1-3] Bivalent or complex-forming univalent counter-ions, on the other hand, are characterised by smaller $\phi_p$ values, as in other systems (see, for instance, ref. 15), the figures in the last lines of Tables 1 and 2 indicating that between 85% and >98% of these species can be inactivated. Comparison of the binding of

[15] Kotliar and Morawetz, *J. Amer. Chem. Soc.*, 1955, **77**, 3692; Wall and Eitel, *ibid.*, 1957, **79**, 1556, 1556; Inagaki, Hotta, and Hirami, *Makromol. Chem.*, 1957, **21**, 1.

magnesium, ethylenediammonium, calcium, and copper makes it obvious that unknown factors play a rôle. Copper possibly forms a complex with the alginate, and the same may happen with silver, the $\phi_p$ value of which is much smaller than that of the other univalent counter-ions.

The intrinsic viscosities, $[\eta]$, of sodium and magnesium alginate solutions [6] show that on addition of permeant salt the polyanion contracts substantially, the ratios ($[\eta]$ salt-free solution) : ($[\eta]$ 0·1M-salt solution) being $>10$. Thus, in the conditions of the Donnan equilibrium measurements, these polyelectrolytes must be characterised by a much more compact configuration than in the conditions of the osmotic tests, where no permeant salts are present. These marked changes in shape do not, however, influence the $\phi_p$ values to any significant extent, as follows from a comparison of the values in Tables 1 and 2. The values in the first two lines of Table 2 show, moreover, that the molecular weight of the alginate has no substantial influence on $\phi_p$. The fraction of " free " sodium or magnesium ions in sodium or magnesium alginate solutions has been found by transference measurements [6] to be larger than the $\phi_p$ values deduced from osmosis. Thus, some of the counter-ions fixed to the alginate under static conditions are removed if migration in an electric field occurs.

It has been suggested [5,6] that bivalent or complex-forming univalent counter-ions are capable of joining together carboxyl groups attached to different alginate chains, and that such intermolecular salt bridges are sufficiently stable to withstand the thermal impact of the solvent. This hypothesis is supported by the observed small $\phi_p$ values. In dilute solutions of polyelectrolytes the probability of intermolecular cross-links is low, but most bivalent and complex-forming univalent counter-ions nevertheless give rise to gel formation which indicates intermolecular bonds. In the case, previously [5] discussed, of alginate fibres the aggregation occurred while the main valency chains were oriented by an external force, so that the cross-linking points were amplified and increased in extension through local crystallisation. It appears that each cross-linked segment undergoes a decrease of solubility, a suggestion which is in accordance with unpublished results of Michaeli who studied solubility changes accompanying the interaction of polyelectrolytes with bivalent counter-ions. It is suggested that stretched, fully swollen alginate fibres, cross-linked, for instance, by calcium ions, contains regions with a high degree of swelling and high mobility of chain segments, alternating with regions in which local precipitation and crystallisation have occurred. The existence of the latter segments was demonstrated by measurements of birefringence and low-angle $X$-ray scattering.[5] If the bivalent counter-ions are replaced by sodium or potassium ions, the $\phi_p$ values of which are larger, a " chemical melting " of the ordered segments in the gel takes place which alters the optical properties,[5] the elasticity,[5] and the overall length.[5] This type of counter-ion replacement may give rise to local solubility increases in those regions of the gel which become less ordered. If, however, the counter-ion exchange is carried out in a poor solvent, *e.g.*, 5N-sodium chloride or 10N-potassium carbonate, over-all dissolution of the gel does not take place.

We are indebted to Dr. Z. Alexandrowicz for the gift of one of his concentration osmometers.

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## 1029. *Isatogens. Part I. Base-catalysed Condensation Products of Methyl and Ethyl* o-*Nitrobenzoylacetate and* o-*Nitrobenzoylacetone.*

By R. T. Coutts, M. Hooper, and D. G. Wibberley.

When suspended in aqueous sodium hydrogen carbonate at room temperature, methyl and ethyl *o*-nitrobenzoylacetate and *o*-nitrobenzoylacetone initially underwent self-condensations finally yielding 2-(1-*o*-nitrophenylvinyl)isatogens. 3,5-Di-*o*-nitrophenyl-5-oxopent-2-enoates and 1,3-di-*o*-nitrophenylhex-3-ene-1,5-dione are further products of the reactions of the esters and the ketone, respectively. Piperidine-catalysed condensation of the *o*-nitrobenzoylacetates with esters of isatogenic or *o*-nitrophenylpropiolic acid also gave the pentenoates, and both they and the diketone were converted into the corresponding isatogens on treatment with pyridine.

In the separation of methyl *o*-nitrobenzoylacetate from its precursor, methyl *o*-nitrobenzoylacetoacetate, by the action of carbon dioxide on the potassium derivative of the crude product [1] it was noticed that the mixture became purple when kept for several hours. To investigate this a suspension of methyl *o*-nitrobenzoylacetate in sodium hydrogen carbonate solution was stirred at room temperature for several days. The same colour change was observed and a purple solid slowly separated. Acidification of the purple filtrate gave orange crystals. The same purple and orange compounds were obtained with concentrations of bicarbonate up to 10·0%; they were obtained also when aqueous solutions of the potassium or the ammonium derivative of methyl *o*-nitrobenzoylacetate were stirred, but not from this ester under the influence of sodium hydroxide or carbonate. No deep colours were produced when methyl *o*-nitrobenzoylacetoacetate, diethyl *o*-nitrobenzoylmalonate, methyl α-*o*-nitrobenzoylpropionate, or ω-cyano-2-nitroacetophenone was stirred with sodium hydrogen carbonate solution; but ethyl *o*-nitrobenzoylacetate and *o*-nitrobenzoylacetone both gave purple and orange compounds similar to those derived from the methyl ester.

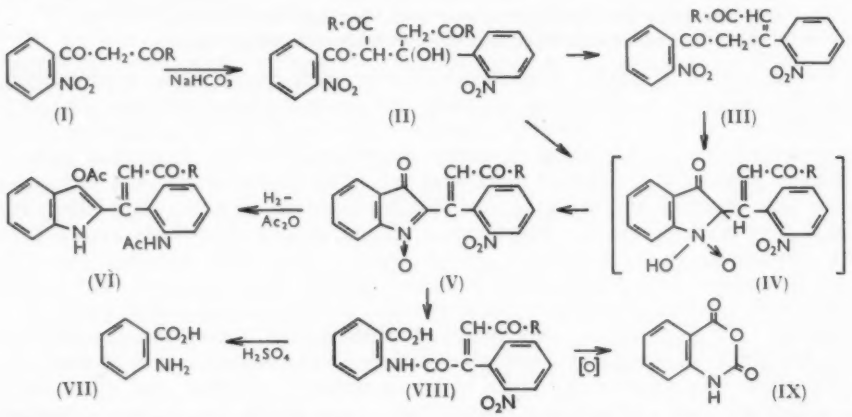
The purple compounds were only sparingly soluble in organic solvents and insoluble in dilute acids; they were soluble in concentrated sulphuric acid and reprecipitated on dilution with water. They were initially insoluble in dilute alkali, but in contact with it all three purple compounds gave the same sequence of colour changes through blue to green, and finally yielded yellow solutions, acidification of which no longer precipitated the purple compounds.

The orange compound from the methyl ester was also isolated as its red piperidinium adduct on reaction of methyl *o*-nitrobenzoylacetate in boiling alcohol, in the presence of piperidine, with methyl or ethyl isatogenate or with methyl or ethyl *o*-nitrophenylpropiolate. None of these reagents gave the red adduct when refluxed with piperidine alone, nor was any such adduct obtained in reactions between methyl *o*-nitrobenzoylacetate and *o*-nitrophenylacetylene or between *o*-nitroacetophenone and methyl isatogenate. The orange compound from the ethyl ester was similarly obtained as its piperidinium adduct by reaction of ethyl *o*-nitrobenzoylacetate with methyl or ethyl isatogenate or with methyl or ethyl *o*-nitrophenylpropiolate. The piperidinium adducts were converted by acid into the orange compounds. The orange compounds were soluble in dilute alkali, giving purple solutions from which they were recovered unchanged on acidification. No purple compounds were isolated on prolonged stirring of the orange compounds with sodium hydrogen carbonate or on treatment with acetic anhydride or sulphuric acid, but this conversion did occur in all three cases when the orange compounds were refluxed in pyridine.

Analyses of the orange compounds indicated in each case the combination of two molecules of the starting material with loss of one methoxycarbonyl, ethoxycarbonyl, or

[1] Coutts, Hooper, and Wibberley, *J.*, 1961, 5058.

acetyl group, and one molecule of water. Analyses of the purple compounds in each case indicated structures containing one molecule of water less than the orange compounds. The expected initial product from the action of aqueous sodium hydrogen carbonate on methyl *o*-nitrobenzoylacetate is the keto-alcohol (II; R = OMe). Hydrolysis of one of the methoxycarbonyl groups followed by decarboxylation and loss of one molecule of water could lead to several structures for the orange compound. We have concluded that the orange compound has structure (III; R = OMe) and that the purple compound has structure (V; R = OMe). The corresponding orange and purple compounds from ethyl *o*-nitrobenzoylacetate have structures (III; R = OEt) and (V; R = OEt), respectively, and those from *o*-nitrobenzoylacetone have structures (III; R = Me) and (V; R = Me).




The infrared spectra of the purple compounds were complex but showed bands in the 1529—1500, 1347—1346, and 863—862 cm.$^{-1}$ regions which could be assigned to the nitro-group or perhaps to the *N*-oxide (cf. Katritzky on spectra of substituted pyridine *N*-oxides [2]), and two bands in the 1724—1684 cm.$^{-1}$ region (carbonyl groups). A band in the 1087—1075 cm.$^{-1}$ region which was also present in methyl isatogenate but absent in the starting materials and orange compounds, and the absence of absorption in the 3600—3000 cm.$^{-1}$ region (OH and NH absent) support the isatogen structure (V). That the purple compounds in fact had this structure was shown by their oxidation, reduction, and hydrolysis. Methyl isatogenate is known [3] to be hydrolysed by alkali to isatin which may be oxidised to, amongst other compounds, isatoic anhydride.[4] We have shown that oxidation of methyl isatogenate with alkaline potassium permanganate yields isatoic anhydride (IX) and that this is also produced, together with *o*-nitrobenzoic acid, by similar oxidation of all three purple compounds. Reduction of 2-pyridylisatogen with zinc and acetic acid in the presence of acetic anhydride yields 3-acetoxy-2-pyridylindole.[5] Analogously the purple compound from *o*-nitrobenzoylacetone yields the indole (VI; R = Me). Heller and Boessneck [6] have shown that methanol and methyl isatogenate in the presence of hydrogen chloride yield an addition product, which loses methanol to re-form the isatogen and is converted by cold sodium hydroxide into *N*-oxalylanthranilic acid. Treatment of an alcoholic suspension of the purple compound (V; R = OMe) with cold sodium hydroxide gave the sequence of colour changes referred to previously, and acidification of the resulting yellow solution liberated a carboxylic acid. If the purple

[2] Katritzky, *Quart. Rev.*, 1959, **13**, 353.
[3] Rodd, "Chemistry of Carbon Compounds," Elsevier, Vol. IV A, p. 90.
[4] Kolbe, *J. prakt. Chem.*, 1884, **30**, 84.
[5] Ruggli and Cuenin, *Helv. Chim. Acta*, 1944, **27**, 649.
[6] Heller and Boessneck, *Ber.*, 1922, **55**, 474.

compound has the isatogen structure (V; R = OMe), then hydrolysis under these conditions, by analogy with the above, could yield the acid (VIII; R = OMe). This structure was supported by the analysis and equivalent weight, and by conversion into anthranilic acid. This material is presumably an intermediate in the permanganate oxidation to isatoic anhydride. A similar acid (VIII; R = Me) was derived by the hydrolysis of 2-(α-acetonylidene-2-nitrobenzyl)isatogen.

The ultraviolet absorption spectra of the orange compounds resembled that of *o*-nitrocinnamic acid, and their infrared spectra showed bands in the 1525—1515, 1355—1345, and 856—855 cm.$^{-1}$ regions (nitro-groups), a band at 1704 cm.$^{-1}$ (carbonyl), and one at 761 cm.$^{-1}$ (*ortho*-disubstituted benzene), but none in the 1087—1075 cm.$^{-1}$ region which had appeared in the purple compounds and methyl isatogenate. The orange colour of this type of compound is to be expected, as is the purple colour of the anion with its increased conjugation. Permanganate oxidation of all three orange compounds yielded *o*-nitrobenzoic acid as the sole isolated product.

Isatogens [7] have been obtained from pyridine or quinoline solutions of several *o*-nitrophenylacetylenes, *o*-nitrostyrenes, and halogenated derivatives thereof by heat or by treatment of their chloroform or benzene solutions with sunlight or nitrosobenzene. The first recorded isatogen, ethyl isatogenate, was isolated by Baeyer [8] by the action of concentrated sulphuric acid on ethyl *o*-nitrophenylpropiolate. There are no references to the preparation of isatogens under conditions such as we have employed, but the formation of indigo by the action of acetone on *o*-nitrobenzaldehyde in the presence of sodium hydroxide [9] or by the action of glucose and sodium hydroxide on *o*-nitrobenzoylacetic acid [10] are both reactions which might well proceed through the intermediate di-isatogen. We suggest that the formation of the isatogen (V) proceeds by attack of the carbanion derived from the ketol (II) on the nitro-group in an analogous manner to the normal carbanion attack on a carbonyl group in an aldol condensation. Reactions in which isatogens are formed are favoured by light; [11] similarly in our experiments a 50% lower yield was obtained in an experiment conducted under identical conditions but in the dark. In the orange compound (III) carbanion formation takes place less readily owing to the absence of the activating COR group, and sodium hydrogen carbonate no longer converts it into the isatogen. The conversion of the orange compounds into the purple compounds, however, did occur with pyridine as catalyst, the conditions being those used in the preparation of isatogens from monohalogenostyrenes.[7] Muth *et al.*[12] have suggested a similar mechanism of carbanion formation from an activated methylene group followed by an aldol-type attack at a nitro-group in their preparation of phenanthridine *N*-oxides from 2-cyanomethyl- or 2-ethoxycarbonylmethyl-2′-nitrobiphenyls. Compounds bearing close structural resemblance to this aldol-type addition compound (IV) are the alcohol adducts of methyl or ethyl isatogenate.[6]

The mechanism for the formation of the orange compounds (III) from the ketols (II) is obvious, but that of their preparation from the piperidine-catalysed reactions of the *o*-nitrobenzoylacetates is at present obscure. The latter reaction, however, does establish which ester group has been removed in the preparation.

The isatogen (V; R = OMe) yielded a mono-oxime, a mononitro-derivative, and an acetone adduct. The analogue (V; R = OEt) gave a similar acetone adduct; the ketone analogue (V; R = Me) gave an isomer on treatment with acetic and hydrochloric acid. The structures of these products have not yet been elucidated but infrared evidence suggests that the isatogen ring remains intact in the oxime and nitro-derivatives.

[7] Sumpter and Miller, "Heterocyclic Compounds with Indole and Carbazole Systems," Interscience Publ. Ltd., London, 1954, p. 154; Smith, *Chem. Rev.*, 1938, **23**, 248.
[8] Baeyer, *Ber.*, 1881, **14**, 1741.
[9] Baeyer and Drewson, *Ber.*, 1882, **15**, 2856.
[10] Overmeyer, *J. Amer. Chem. Soc.*, 1926, **48**, 456.
[11] Splitter and Calvin, *J. Org. Chem.*, 1955, **20**, 1086.
[12] Muth, Ellers, and Folmer, *J. Amer. Chem. Soc.*, 1957, **79**, 6500.

## Experimental

Infrared spectra (KBr disc) were determined by Mr. G. S. Hall, Grubb-Parsons Ltd., Newcastle upon Tyne. Equivalent weights were determined, except where otherwise stated, by potentiometric back-titrations.

2-(α-*Methoxycarbonylmethylene-2-nitrobenzyl*)*isatogen* (V; R = OMe).—A suspension of methyl *o*-nitrobenzoylacetate (2·0 g.) in 5·0% aqueous sodium hydrogen carbonate (20·0 ml.) was stirred at room temperature for 4 days. Within several hours the solution became purple; after one day the purple *product* (V; R = OMe) had separated and after 3 days no unchanged ester was visible. The solid (0·15 g.) was collected; it recrystallised from aqueous acetone as purple prisms, m. p. 242—243° (decomp.) (Found: C, 61·7; H, 3·4; N, 8·0; OMe, 8·75. $C_{18}H_{12}N_2O_6$ requires C, 61·4; H, 3·4; N, 8·0; OMe, 8·8%), $\nu_{max.}$ 1724s and 1710(sh)m (C=O), 1529s ($NO_2$), 1346s ($NO_2$), 1075s (this band was only present in spectra of isatogen derivatives but no assignment could be made), 862w (C–$NO_2$), 761m cm.$^{-1}$ (*ortho*-disubstituted benzene or $NO_2$ [13]). Methyl isatogenate has $\nu_{max.}$ 1730s and 1703s (C=O), 1504s, 1075m, 860w (C–N), 761m cm.$^{-1}$ (*ortho*-disubstituted benzene).

Stirring aqueous solutions of the potassium or ammonium derivative of methyl *o*-nitrobenzoylacetate gave the same isatogen, m. p. 242—243° (decomp.), in 10—15% yields.

A repetition of the first preparation in a blackened flask gave the same isatogen (0·07 g.), m. p. 242—243° (decomp.).

The compound (V; R = OMe) was insoluble in dilute acid or alkali, and sparingly soluble in acetone and acetic acid, but insoluble in most other organic solvents. It was recovered unchanged after dissolution in concentrated sulphuric acid and reprecipitation with water. A suspension in aqueous acetone or ethanol, on treatment with sodium hydroxide at room temperature, rapidly underwent colour changes from purple to deep blue, to green, and finally to yellow.

*Methyl* 3,5-*Di*-o-*nitrophenyl*-5-*oxopent*-2-*enoate* (III; R = OMe).—The purple filtrate remaining after removal of the isatogen in the first of the preceding experiments was acidified with hydrochloric acid, and the liberated oil was extracted in ether, recovered (1·5 g.), and dissolved in ethanol (4·5 ml.). During 2 days at room temperature the solution deposited pale orange prisms (0·11 g.) of the *ester* (III; R = OMe), m. p. 162—164° (decomp.), m. p. 165—166° (decomp.) (from acetic acid) (Found: C, 58·5; H, 3·5; N, 7·4; OMe, 8·4. $C_{18}H_{14}N_2O_7$ requires C, 58·4; H, 3·8; N, 7·6; OMe, 8·4%), $\lambda_{max.}$ 235 (log ε 4·42), 273 mμ (log ε 4·41) [cf. *o*-nitrocinnamic acid, $\lambda_{max.}$ 228 (log ε 4·0), 310 mμ (log ε 4·25)], $\nu_{max.}$ 1704s (C=O), 1525s ($NO_2$), 1355s ($NO_2$), 855vw (C–$NO_2$), and 761m cm.$^{-1}$ (*ortho*-disubstituted benzene or $NO_2$). Acidification of the filtrates remaining after removal of the isatogen from the reactions of the potassium and ammonium derivatives of methyl *o*-nitrobenzoylacetate gave, after crystallisation, the same orange compound, m. p. 165—166° (decomp.). It was insoluble in dilute acid but soluble in most organic solvents; in dilute alkali it gave a deep purple solution and was recovered unchanged on acidification. Boiling the alkaline solutions removed the colour, after which acidification no longer precipitated the orange compound.

2-(α-*Ethoxycarbonylmethylene-2-nitrobenzyl*)*isatogen* (V; R = OEt).—In the manner described above for the methyl ester, ethyl *o*-nitrobenzoylacetate (2·0 g.) with 2·0% sodium hydrogen carbonate solution yielded after 11 days the *isatogen* (V; R = OEt) (0·47 g.), crystallising from aqueous acetone in deep reddish-purple prisms, m. p. 197—198° (decomp.) (Found: C, 62·7; H, 4·2; N, 7·7; OEt, 13·0. $C_{19}H_{14}N_2O_6$ requires C, 62·3; H, 3·8; N, 7·7; OEt, 12·3%). This had solubilities similar to those of the methyl analogue and gave the same sequence of colour changes on treatment of its suspension in aqueous acetone with sodium hydroxide.

*Ethyl* 3,5-*Di*-o-*nitrophenyl*-5-*oxopent*-2-*enoate* (III; R = OEt).—Acidification with acetic acid of the purple filtrate left after removal of the preceding isatogen gave an orange oil from which the *pentenoate* (0·16 g.) was isolated by crystallisation from aqueous acetic acid. Recrystallisation yielded orange prisms, m. p. 136—137° (decomp.) (Found: C, 59·1; H, 3·65; N, 7·6; OEt, 11·7%; equiv., 382. $C_{19}H_{16}N_2O_7$ requires C, 59·4; H, 4·2; N, 7·3; OEt, 11·7%; equiv., 384).

2-(α-*Acetonylidene*-2-*nitrobenzyl*)*isatogen* (V; R = Me).—As described for methyl *o*-nitrobenzoylacetate, *o*-nitrobenzoylacetone (4·0 g.) with 5·0% aqueous sodium hydrogen carbonate

[13] Cross, " Introduction to Practical Infra-Red Spectroscopy," Butterworths, London, 1960, p. 70.

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(40 ml.) yielded after 5 days the *isatogen* (V; R = Me) (1·81 g.), crystallising from aqueous acetone in deep violet prisms, m. p. 242—243° (decomp.) (Found: C, 63·8; H, 3·5; N, 8·0; OMe, 0. $C_{18}H_{12}N_2O_5$ requires C, 64·3; H, 3·6; N, 8·3%), $\nu_{max.}$ 1699m and 1684m (C=O), 1520s ($NO_2$), 1347s ($NO_2$), 1087s, 863w (C–$NO_2$), 752m cm.$^{-1}$ (*ortho*-disubstituted benzene or $NO_2$). The mixed m. p. with the isatogen (V; R = OMe) was depressed by only one degree, and the product showed similar solubilities and sequence of colour changes. This isatogen gave a positive iodoform reaction.

**1,3-*Di*-o-*nitrophenylhex*-3-*ene*-1,5-*dione*** (III; R = Me).—Acidification of the purple filtrate after removal of the preceding isatogen yielded, after washing with ether, a *diketone* (III; R = Me) (0·53 g.) which crystallised from acetic acid in orange prisms, m. p. 185—186° (decomp.) (Found: C, 61·1; H, 3·5; N, 7·9; OMe, 0·5%; equiv., 351. $C_{18}H_{14}N_2O_6$ requires C, 61·0; H, 3·95; N, 7·9%; equiv., 354), $\lambda_{max.}$ 239 (log ε 4·35), 280 mμ (log ε 4·35), $\nu_{max.}$ 1704s (C=O), 1515s ($NO_2$), 1345s ($NO_2$), 856vw (C–$NO_2$), 761m cm.$^{-1}$ (*ortho*-disubstituted benzene or $NO_2$).

*Reactions of the Isatogen* (V; R = OMe).—(a) *Oxidation.* The isatogen (0·25 g.) in 5·0% sodium hydroxide (20 ml.) was refluxed with potassium permanganate (3 × 0·5 g.) for 15 min. Methanol was added to reduce the last traces of permanganate, the mixture filtered, and the residual manganese dioxide washed with boiling water. The combined filtrate and washings were acidified with hydrochloric acid, and the resulting suspension extracted with ether. Evaporation of the extract gave the crude product which was extracted with boiling water. The aqueous extract, on cooling, gave *o*-nitrobenzoic acid (0·012 g.), m. p. and mixed m. p. 146—147°. The residue, insoluble in boiling water, crystallised from acetic acid, yielding isatoic anhydride (IX) (0·008 g.), m. p. 233—234° alone and undepressed on admixture with a sample of the product isolated in a similar manner on permanganate oxidation of methyl isatogenate.

(b) *Hydrolysis.* A suspension of the isatogen (0·3 g.) in ethanol (10·0 ml.) was stirred with 20% aqueous sodium hydroxide (2·0 ml.) for 15 min. at room temperature. The resulting clear yellow solution was acidified with hydrochloric acid, and the precipitated solid extracted in ether (2 × 20 ml.). Concentration of the extract gave **2-(β-*methoxycarbonyl*-α-o-*nitrophenyl*-*acrylamido*)*benzoic acid*** (0·17 g.) which crystallised from ethanol in pale yellow prisms, m. p. 213—214° (decomp.) [Found: C, 58·6; H, 3·8; N, 7·7%; equiv. (titration in neutral acetone), 368. $C_{18}H_{14}N_2O_7$ requires C, 58·4; H, 3·8; N, 7·6%; equiv., 370].

This acid (0·05 g.) was refluxed with 30% sulphuric acid (1·0 ml.) for 90 min. The oil then present was removed by extraction with ether and the aqueous layer adjusted to pH 5·0 with sodium hydroxide and then acetic acid. The resulting suspension was extracted with ether, and the extract evaporated to dryness. The residue (0·01 g.), on crystallisation from water, had m. p. 140—142° alone or mixed with anthranilic acid. It yielded the characteristic red colour (given by anthranilic acid) on fusion with calcium chloride and dissolution in ethanol.

(c) *Oxime.* The isatogen (V; R = OMe) with hydroxylamine hydrochloride and pyridine in ethanol yielded the oxime, crystallising from ethanol in bright yellow needles, m. p. 159—160° (decomp.) (Found: C, 58·5; H, 3·4; N, 11·4. Calc. for $C_{18}H_{13}N_3O_6$: C, 58·85; H, 3·5; N, 11·4%).

(d) *Nitration.* The isatogen (0·08 g.) was heated in concentrated nitric acid (5·0 ml.) at 70—80° for 10 min. (colour change from deep red to orange). Cooling and dilution with water precipitated a *mononitro-derivative* (0·05 g.), orange prisms (from benzene), m. p. 221—223° (decomp.) (Found: C, 55·0; H, 3·2; N, 10·8. $C_{18}H_{11}N_3O_8$ requires C, 54·4; H, 2·8; N, 10·6%), $\nu_{max.}$ 1724m (C=O), 1520s ($NO_2$), 1345s and 1327(sh)s ($NO_2$), 1093s, 855vw ($NO_2$), 746w cm.$^{-1}$ (*ortho*-disubstituted benzene or $NO_2$).

(e) *Acetone adduct.* A suspension of the isatogen (0·1 g.) in acetone (3·0 ml.) and water (3·0 ml.) was stirred with 20% sodium hydroxide solution (0·4 ml.) for 15 min. at room temperature. The final clear yellow solution was acidified with acetic acid, depositing pale yellow prisms of the *adduct* (0·09 g.), m. p. 171—172° (from acetic acid) (Found: C, 61·3; H, 4·3; N, 6·4; OMe, 7·0. $C_{21}H_{18}N_2O_7$ requires C, 61·4; H, 4·4; N, 6·8; OMe, 7·6%).

*Additional Syntheses of Methyl* **3,5-*Di*-o-*nitrophenyl*-5-*oxopent*-2-*enoate***.—(*a*) Methyl *o*-nitrobenzoylacetate (0·25 g.), methyl *o*-nitrophenylpropiolate (0·2 g.), piperidine (0·1 ml.), and ethanol (4·0 ml.) were refluxed for 1 hr. The bright red *piperidinium adduct* (0·18 g.), m. p. 176—177° (decomp.), which separated was collected (Found: C, 60·5; H, 5·1. $C_{23}H_{25}N_3O_7$ requires C, 60·7; H, 5·5%). Boiling dilute hydrochloric acid converted it quantitatively into the methyl ester (III; R = OMe), m. p. and mixed m. p. 165—166° (decomp.).

Piperidinium hydrochloride, m. p. and mixed m. p. 236—237°, was isolated from the filtrate. The same piperidinium adduct was isolated in similar reactions between methyl *o*-nitrobenzoylacetate and (*b*) ethyl *o*-nitrophenylpropiolate, (*c*) methyl isatogenate, or (*d*) ethyl isatogenate. In all cases treatment with dilute acid or crystallisation from acetic acid gave the free ester.

*Oxidation of Methyl* 3,5-*Di*-o-*nitrophenyl*-5-*oxopent*-2-*enoate*.—The ester (0·25 g.) in sodium hydroxide solution with potassium permanganate gave, as the sole isolated product, *o*-nitrobenzoic acid (0·08 g.), m. p. and mixed m. p. 146—147°.

*Conversion of the Pentenoate* (III; R = OMe) *into the Isatogen* (V; R = OMe).—The ester (0·1 g.) was heated in pyridine (1·0 ml.) on the water bath for 1 hr., then poured into water (20 ml.), and the precipitated compound (0·03 g.) was collected (centrifuge). Crystallisation from acetic acid gave purple prisms, m. p. and mixed m. p. 242—243°.

*Acetone Adduct of* 2-(α-*Ethoxycarbonylmethylene*-2-*nitrobenzyl*)*isatogen*.—Treatment of the isatogen (V; R = OEt) (0·085 g.) with acetone and sodium hydroxide as above gave the acetone *adduct* (0·07 g.) crystallising from acetic acid in orange prisms, m. p. 166—167° alone and 150—153° on admixture with the previous acetone adduct (Found: N, 6·5. $C_{22}H_{20}N_2O_7$ requires N, 6·6%).

*Additional Syntheses of Ethyl* 3,5-*Di*-o-*nitrophenyl*-5-*oxopent*-2-*enoate* (III; R = OEt).—By reactions similar to those employed for the methyl ester, ethyl *o*-nitrobenzoylacetate was caused to react with methyl and ethyl *o*-nitrophenylpropiolate and with methyl and ethyl isatogenate. From all four reactions a red piperidinium adduct was isolated and converted, by treatment with acid, into the ester (V; R = OEt), m. p. and mixed m. p. 136—137°.

*Conversion of the Ester* (III; R = OEt) *into the Isatogen* (V; R = OEt).—The ester (0·1 g.) was refluxed in pyridine for 1 hr. and then diluted, to yield the isatogen (0·039 g.), m. p. (from acetic acid) and mixed m. p. 197—198° (decomp.).

*Reactions of* 2-(α-*Acetonylidene*-2-*nitrobenzyl*)*isatogen*.—(a) *Oxidation*. The isatogen (0·25 g.) with alkaline potassium permanganate gave *o*-nitrobenzoic acid (0·016 g.), m. p. and mixed m. p. 145—146°, and isatoic anhydride (0·019 g.), m. p. and mixed m. p. 233—234°.

(b) *Reduction*. The isatogen (0·5 g.), acetic acid (20 ml.), acetic anhydride (15 ml.) and zinc dust (3·0 g.) were refluxed for 90 min. The resulting solution was treated with ethanol (20 ml.) and evaporated to dryness, and the residue extracted with benzene. The extract was evaporated to give the 3-*acetoxy*-2-(2-*acetamido*-α-*acetonylidenebenzyl*)*indole* (VI; R = Me) (0·26 g.) which crystallised from benzene in fawn prisms, m. p. 289—291° (decomp.) (Found: C, 70·45; H, 5·2; N, 7·6. $C_{22}H_{20}N_2O_4$ requires C, 70·2; H, 5·3; N, 7·45%).

(c) *Hydrolysis*. The isatogen (0·1 g.) was hydrolysed with cold sodium hydroxide solution as above. o-(2-o-*Nitrophenyl*-4-*oxopent*-2-*enamido*)*benzoic acid* (VIII; R = Me) (0·05 g.) crystallised from ethanol in pale yellow prisms, m. p. 239—240° (decomp.) (Found: C, 60·9; H, 4·2; N, 7·3. $C_{18}H_{14}N_2O_6$ requires C, 61·0; H, 3·95; N, 7·9%).

*Isomerisation of the Isatogen* (V; R = Me).—The isatogen (0·1 g.), acetic acid (5·0 ml.), and hydrochloric acid (5·0 ml.) were refluxed for 2·5 hr. The resulting clear red solution was filtered and diluted with water (15 ml.). A trace of unchanged isatogen was removed and the filtrate set aside. The pale pink solid *isomer* which separated was purified by precipitation from its solution in sodium carbonate with dilute acid. Crystallisation from acetic acid gave pale cream needles, m. p. 255—256° (decomp.) (Found: C, 63·6; H, 3·9; N, 8·35. $C_{18}H_{12}N_2O_5$ requires C, 64·3; H, 3·6; N, 8·3%).

*Oxidation of the Diketone* (III; R = Me).—The diketone (0·25 g.), on oxidation with alkaline permanganate, gave, as the sole isolated product, *o*-nitrobenzoic acid (0·08 g.), m. p. and mixed m. p. 145—146°.

*Conversion of the Diketone* (III; R = Me) *into the Isatogen* (V; R = Me).—The diketone (0·2 g.) was refluxed in pyridine for 1 hr. and diluted with water, to yield the isatogen (0·065 g.), m. p. (from acetic acid) and mixed m. p. 242—243°.

We thank Mrs. A. Why and Mr. D. Wilson for technical assistance.

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XUM

**1030.** *Organic Reactions in Aqueous Solution at Room Temperature. Part II.* The Influence of* pH *on Condensations involving the Linking of Carbon to Carbon, of Carbon to Nitrogen, and of Carbon to Sulphur.*

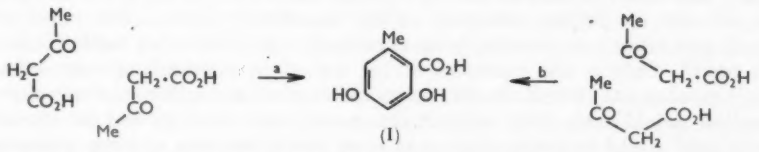
By J. R. Bethell and P. Maitland.

Further simple reactions under "physiological" ("cell-possible") conditions are described, leading to the formation of the benzene, the pyrazole, and the thiazole ring system. Two examples of the Michael reaction under mild conditions are given.

In continuation of our investigations designed to broaden the field known as "syntheses under physiological (or 'cell-possible') conditions" in relation to both biogenetic problems and general organic synthetical methods, some further simple model condensations in aqueous solution at room temperature over pH ranges have been examined. The reaction conditions employed were similar to those used before. Water-soluble reactants were chosen so that, on reaction, water-insoluble crystalline products were precipitated in a pure or nearly pure state, and were isolated directly from the reaction mixture by filtration, the usual losses thus being avoided. The permissible physiological pH range was discussed in Part I, and the conclusion reached that it might be as wide as 1·5—11. All the reactions investigated in this present work were found to proceed somewhere within this range.

The work is described below in four sections, according to the type of condensation employed, namely, C–C ⟶ a benzene derivative, C–C + C–N (Michael reaction), C–N ⟶ a pyrazole derivative, and C–S and C–N ⟶ a thiazole derivative. No evidence has been adduced in any of the sections for an exact scheme of biogenesis, which must come ultimately from specific biochemical investigations: but, with the exception of one reactant, all the condensations were carried out with substances either already known in Nature or containing naturally occurring groups.

(a) *Double* C–C *Claisen–Knoevenagel Condensation of Two* $C_3$ *Aliphatic Units, to give a Benzene Derivative.*—Robinson has long held the opinion that the readily formed, stable, benzene nucleus is very unlikely to be formed in Nature by only a single route.[1] He noted [2] the occurrence of erythritol in certain lichens as an ester of orsellinic acid (I), and suggested for the latter an origin from the condensation of two $C_4$ units, which might



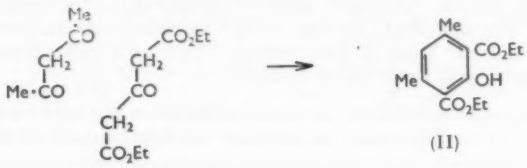

be acetoacetic acid, by route a or b. We have investigated a condensation of type (Ia). However, acetoacetic acid is too unstable and the ethyl ester has never been shown to undergo self-condensation in this manner. In Part I it was shown that furfuraldehyde, with its very active aldehyde group, condensed with the very active methylene group of acetylacetone to give furfurylideneacetylacetone in 60—76% yield over the pH range 3·6—6·5, supporting the acid-catalysed mechanism for Claisen–Knoevenagel reactions. The present model, which might be formed by a double Claisen–Knoevenagel condensation of the symmetrical $C_3$–$C_3$ type as in (Ia), was diethyl 2-hydroxy-4,6-dimethylisophthalate

* Part I, *J.*, 1951, 3155.

[1] Sir Robert Robinson, "The Structural Relations of Natural Products," Clarendon Press, Oxford, 1955, p. 30.

[2] Madrid Lecture, IX Congr. Internat. Union Pure Appl. Chem., 1934, p. 6; ref. 1, p. 8.

(II), prepared by condensing acetylacetone with diethyl acetonedicarboxylate. This reaction was first described by Prelog *et al.*,[3] who used alcoholic sodium ethoxide at room temperature. Similar condensations have been performed by using piperidine in boiling alcohol,[4] or an aqueous-alcoholic glycine–piperidine buffer at pH 7 at room temperature.[5] The original condensation, to give the ester (II), was repeated but in saturated buffered aqueous solution, and Table 1 shows that the phenol was formed in the pH range 5·6—9·2, the highest yield (86%) of pure product being precipitated at pH 7·3—7·6.



(II)

Unlike the simpler example of furfurylideneacetylacetone above, this condensation can therefore proceed by the acid- or base-catalysed mechanisms; and the fact that it takes place within the physiological pH range supports the possible origin of some natural benzene derivatives by a $C_3 + C_3$ route of this type.

TABLE 1.

Diethyl 2-hydroxy-4,6-dimethylisophthalate (II) from acetylacetone (1·00 g.) in buffer solution (N-$KH_2PO_4$–N-NaOH) (20 ml.) and diethyl acetonedicarboxylate (2·02 g.) in buffer solution (180 ml.); 5 and 12 days at room temp. M. p. 43—44° (pure).

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Initial pH ..... | 4·5[a] | 5·6 | 6·2 | 6·8 | 7·3 | 7·6[b] | 8·2 | 8·6 | 9·2 | 11·0 |
| Final pH[c] ..... | 4·5 | 5·7 | 6·3 | 6·8 | 7·3 | 7·7 | 8·2 | 8·5 | 8·7 | 10·0 |
| Yield (g.) (5 days) ... | 0 | 0·15 | 0·85 | 1·72 | 2·16 | 2·20 | 2·08 | 1·71 | 1·01 | 0·0 |
| Yield (g.) (12 days) | 0 | 0·88 | 1·55 | 2·10 | 2·29 | 2·28 | 2·08 | 1·71 | 1·01 | 0·0 |
| Yield (%) (12 days) | 0 | 26 | 58 | 79 | 86 | 86 | 78 | 64 | 38 | 0 |
| M. p. ..... | | 42—43° | ◄ | ◄ | ◄ | 43—44° | ► | ► | ► | |

[a] Natural pH of the mixed aqueous solutions. [b] As a quicker preparative method, at this optimum pH a yield of 77% may be obtained after 2 days. [c] pH measured after five days.

(b) *The Michael Reaction* (*Cyanoethylation*). C–C *Condensation of Methyl Acetoacetate and Vinyl Cyanide, and* C–N *Condensation of Aniline and Vinyl Cyanide.*—In the Michael reaction [6,7] the usual conditions are to heat the reactants in anhydrous solvents with sodium ethoxide or similar catalysts.[8] Only occasionally have acidic catalysts been employed, and usually under anhydrous conditions. In some cases neither solvent nor heat is used.[9] Only a few examples of the use of aqueous solvents are known.[10,11] Kamlet [11] pointed out that if the ionisation constant of the addendum was high, then the reaction should take place without the usual basic catalyst, and he showed that barbituric acid added to β-nitrostyrene at room temperature in aqueous mixtures with dioxan, methanol, or acetic acid. Since the Michael reaction, if it could be shown to

[3] Prelog, Metzler, and Jeger, *Helv. Chim. Acta*, 1947, **30**, 675.
[4] *J. Org. Chem.*, 1958, **23**, 34.
[5] Mühlemann, Festshrift Paul Casparis, 1949, p. 159; *Chem. Abs.*, 1951, **45**, 596.
[6] (*a*) Henecka, "Chemie der Beta-dicarbonylverbindungen," Springer-Verlag, 1950, p. 243; (*b*) *Org. Reactions*, 1959, **10**, 179.
[7] Arndt, Scholz, and Frobel, *Annalen*, 1935, **521**, 111.
[8] Hickinbottom, "Reactions of Organic Compounds," Longmans Green, 3rd edn., 1957, p. 48; ref. 6(*b*), p. 264.
[9] Kloetzel, *J. Amer. Chem. Soc.*, 1947, **69**, 2271; Leonard and Shoemaker, *ibid.*, 1949, **71**, 1876; Dreiding and Tomasewski, *ibid.*, 1955, **77**, 411.
[10] Ikawa, Stahmann, and Link, *J. Amer. Chem. Soc.*, 1944, **66**, 902; McKinney *et al.*, *ibid.*, 1950, **72**, 2599; 1951, **73**, 1643; Herzog, Gold, and Geckler, *ibid.*, 1951, **73**, 749; Shechter and Zeldin, *ibid.*, 1951, **73**, 1276; Jung and Cordier, *Compt. rend.*, 1959. **249**, 711.
[11] Kamlet, *J. Amer. Chem. Soc.*, 1955, **77**, 4896; *ibid.*, 1956, **78**, 4556.

proceed under sufficiently mild conditions, might merit consideration in biogenetic problems, it was decided to study the influence of pH on two examples of cyanoethylation.[12]

(i) *Methyl acetoacetate and vinyl cyanide.* Bruson and Riener condensed one mol. of methyl acetoacetate with two mol. of vinyl cyanide, obtaining methyl αα-di-(2-cyanoethyl)-acetoacetate (III) by reaction in dioxan containing Triton B at 30—40°; they obtained a yield (crude) of 50%. We also used methyl acetoacetate since it is much more soluble

$$2CH_2{:}CH{\cdot}CN + CH_3{\cdot}CO{\cdot}CH_2{\cdot}CO_2Me \longrightarrow CH_3{\cdot}CO{\cdot}C(CH_2{\cdot}CH_2{\cdot}CN)_2{\cdot}CO_2Me \quad (III)$$

in water (38%) than the ethyl ester (14·3%), and the solubility of vinyl cyanide in water (7·3%) made it also suitable. Our study (Table 2) shows that the ester (III) was obtained within the approximate pH range 7·7—11·5. It was impossible, even when large amounts of buffer were used, to keep the pH constant during the 6-day period; this was probably due to hydrolysis. The product was precipitated in analytically pure state from the

TABLE 2.

Diethyl αα-di-(2-cyanoethyl)acetoacetate (III) from methyl acetoacetate (2·32 g.) in buffer solution (N-$KH_2PO_4$–N-NaOH) (10 ml.) and vinyl cyanide (2·12 g.) in buffer solution (40 ml.); 6 days at room temp. M. p. 154—156° (pure; all products).

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Initial pH ..... | 7·7 | 9·0 | 9·5 | 10·0 | 10·5 | 10·7 | 10·9 | 11·5 | 12·0 |
| Final pH ..... | 7·3 | 7·6 | 7·8 | 7·9 | 8·0 | 9·7 | 10·0 | 10·3 | 10·0 |
| Yield (%) ..... | Trace | 7 | 13 | 23 | 44 | 46 | 45 | 26 | — |

reaction mixture; the maximum yield (46%) was obtained at pH 10·7, falling to 9·7, *i.e.*, still within the physiological pH range. There was no trace of the monocyanoethylated product. No product was obtained in acid solution, which shows that this Michael reaction can only proceed by the base-catalysed mechanism.

(ii) *Aniline and vinyl cyanide.* Ammonia and many amines have been added to vinyl cyanide, but the conditions for addition vary from room temperature without a catalyst to an autoclave at high temperatures in presence of catalysts. In the present example, aniline was chosen as it has appreciable solubility (3·4%) in water and was known to give crystalline mono- and di-adducts, *N*-2-cyanoethyl- and *NN*-di-(2-cyanoethyl)-aniline. Cookson and Mann [14] found that aniline does not combine appreciably with boiling vinyl cyanide in the presence of sodium methoxide or acetic acid, but in acetic acid at 150° (autoclave) a mixture of mono- and di-adduct was produced. Bekhli and Serebrennikov [15] obtained a 98% yield of monoadduct by heating aniline, aniline acetate, and vinyl cyanide at 120—140°. Cymerman-Craig and Moyle [16] heated aniline hydrochloride and vinyl cyanide with diethylamine at 180° and obtained the monoadduct in 72—78% yield. Heininger [17] heated the reactants with cupric acetate monohydrate and obtained a 73% yield of the same product.

When saturated aqueous buffered solutions of aniline and vinyl cyanide were mixed, an oil was first deposited, which slowly crystallised to give the monoadduct uncontaminated with diadduct even in presence of an excess of vinyl cyanide. More dilute solutions favoured more rapid crystallisation but the yields decreased, so an optimum dilution with both factors in mind had to be employed. Table 3 shows that pure product was precipitated over the pH range 5·1—11·6, with a maximum yield of 44—45% in the pH range 7·5—10, except around pH 9·2 where there was a repeatable but unaccountable decrease of 5—6%.

Although the duration of the actual experiment was 20 days (to allow for complete precipitation), equimolar quantities of aniline and vinyl cyanide in the buffer solution

[12] Bruson, *Org. Reactions*, 1954, **5**, 79.
[13] Bruson and Riener, *J. Amer. Chem. Soc.*, 1942, **64**, 2850.
[14] Cookson and Mann, *J.*, 1949, 67.
[15] Bekhli and Serebrennikov, *Zhur. obschei Khim.*, 1949, **19**, 1553; *Chem. Abs.*, 1950, **44**, 3448.
[16] *Org. Synth.*, 1956, **36**, 6.
[17] Heininger, *J. Org. Chem.*, 1957, **22**, 1213.

TABLE 3.

*N*-2-Cyanoethylaniline from vinyl cyanide (1·06 g.) in buffer solution (50 ml.) and aniline (1·86 g.) in buffer solution (150 ml.); 20 days at room temperature. M. p. 50—51° (pure).

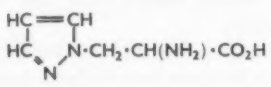
| Buffer | N-AcOH–N-NaOAc | | N-$KH_2PO_4$–N-NaOH | | | | | |
|---|---|---|---|---|---|---|---|---|
| Initial and final pH ... | 4·2 | 5·1 | 6·1 | 6·8 | 7·5 | 8·0 | 8·3 | 8·8 |
| Yield (%) [a] ..... | — | 23 | 38 | 42 | 44 | 44 | 45 | 44 |

| Buffer | N-$KH_2PO_4$–N-NaOH | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Initial and final pH ... | 9·2 | 9·7 | 10·0 | 10·4 | 10·8 | 11·0 | 11·6 | 11·9 |
| Yield (%) [a] ..... | 39 | 45 | 45 | 43 | 43 | 39 | 17 | — |

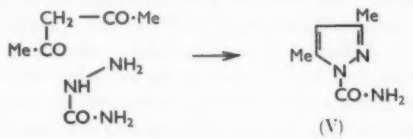
[a] All products were slightly coloured, even when the experiments were performed in nitrogen, but they melted at 50—51° and gave correct analyses.

at pH 8·8 gave a 29% yield after 7 days; using double the quantity of vinyl cyanide under the same conditions gave a 59% yield (calculated on aniline).

(c) C–N *Condensation to give a Pyrazole Derivative.*—Only one naturally occurring pyrazole derivative (IV) is known.[18] There has been as yet no approach to the biogenesis of the pyrazole ring system. Most of the methods already known for synthesising the system [19] involve intermediates and conditions unlikely to obtain in a cell. One method which offered the possibility of mild conditions was the condensation of β-dicarbonyl compounds with hydrazines; the latter have not been reported in Nature, but seem not unlikely cell intermediates. 3,5-Dimethylpyrazole-1-carboxyamide (V), prepared by



(IV)



(V)

condensation of acetylacetone and semicarbazide,[20] proved to be suitable for a pH study (Table 4). The pyrazole (V) was formed in the pH range 4·1—8·2, the highest yield of pure product (86%) being precipitated at pH 4·1 and diminishing to 17% at pH 8·2 and

TABLE 4.

3,5-Dimethylpyrazole-1-carboxyamide (V) from semicarbazide hydrochloride (2·20 g.) and acetylacetone (2·00 g.) in buffer solution (70 c.c.) (N-$KH_2PO_4$–N-NaOH). M. p. 111—113° (pure; all products).

| Initial pH ... | 4·1 | 4·4 | 4·8 | 5·3 | 5·8 | 6·4 | 7·1 | 7·5 | 8·1 | 8·2 | 10 |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Final pH ... | 4·6 | 4·6 | 4·9 | 5·3 | 5·6 | 6·2 | 6·7 | 6·9 | 7·4 | 7·3 | — |
| Duration: [a] | 2h | 2h | 3h | 6h | 1d | 2d | 2d | 5d | 12d | 12d | 7d |
| Yield (%) ... | 86 | 85 | 83 | 80 | 76 | 64 | 49 | 40 | 31 | 17 | 0 |

[a] h = hours; d = days.

nil at pH 10. The duration of the experiments to obtain the maximum yield at each pH varied greatly, from 2 hours at pH 4·1 to 12 days at pH 8·2. Below pH 4, hydrolysis and decarboxylation to 3,5-dimethylpyrazole was observed.

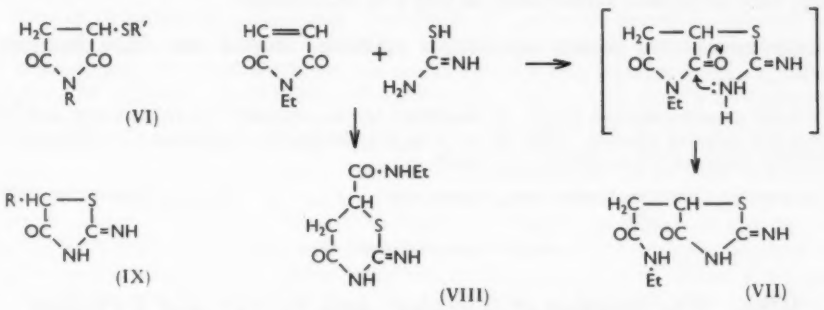
(d) *Combination of* C–S *and* C–N *Condensations to give a Thiazole Derivative.*—Only

[18] Fowden, Noe, Ridd, and White, *Proc. Chem. Soc.*, 1959, 131; Noe and Fowden, *Nature*, 1959, **184**, B.A. Suppl., 69; *Biochem. J.*, 1960, **77**, 543; Sugimoto, Watanabe, and Ide, *Tetrahedron*, 1960, **11**, 231.

[19] Thorpe's "Dictionary of Applied Chemistry," 1950, Vol. X, p. 291; Rodd, "Chemistry of the Carbon Compounds," Elsevier, 1957, Vol. IVA, p. 245; Elderfield, "Heterocyclic Compounds," John Wiley and Sons, 1957, Vol. V, p. 47.

[20] Posner, *Ber.*, 1901, **34**, 3973.

a few of the many syntheses of the thiazole ring system [21] might be of biogenetic significance. An unexpected synthesis was discovered by Marrian,[22] who referred to the possible biological importance of the addition of certain thiols to maleimides, and later [23] investigated the action of these imides with the incipient thiol group of thioureas. The normal thiols yielded products of the type (VI), in which simple addition takes place across the double bond. This was proved by treatment with Raney nickel, which caused



fission across the S–C bond, resulting in a succinimide derivative. In contrast to this, thioureas produced compounds which he showed might contain a five-membered (VII) or a six-membered ring (VIII). He prepared the compound in 69·5% yield in aqueous alcohol at room temperature. This reaction was found to be suitable for a pH study.

When buffer solutions of *N*-ethylmaleimide and thiourea were mixed, the product, proved below to be the thiazolidone (VII), was precipitated in pure, or nearly pure state, over the pH range 2·6—7·9, the highest yield (74%) of pure product being obtained at pH 5·6 (see Table 5). The rapid decline in the yield on the alkaline side is probably due to hydrolysis of the imide.[24]

TABLE 5.

*N*-Ethyl-α-(2-imino-4-oxothiazolidin-5-yl)acetamide (VII) from *N*-ethylmaleimide (0·625 g.) in buffer solution (35 c.c.) and thiourea (0·38 g.) in buffer solution (5 c.c.); 2 days at room temperature. M. p. 210—212° (pure).

| Buffer | N-HCl–N-NaOAc | | N-AcOH–N-NaOAc | | | N-$KH_2PO_4$–N-NaOH | | |
|---|---|---|---|---|---|---|---|---|
| Initial pH | 2·6 | | 3·8 | 4·5 | 5·6 | 6·8 | 7·9 | 8·8 |
| Final pH | 2·6 | | 3·8 | 4·5 | 5·6 | 6·7 | 7·6 | 7·9 |
| Yield (%) [a] | 37 | | 59 | 72 | 74 | 63 | 14 | Trace |
| M. p.[b] | 209—210° | | | 210—212° | | 209—211° | 207—208° | |

[a] Monohydrate. [b] Inserted at 190° and heated rapidly. Slow heating gives m. p. 195°, as Marrian noted.

For a structural study of the product, 2-imino-4-oxothiazolidin-5-ylacetic acid [25] (IX; R = $CH_2$·$CO_2H$) and 2-iminothiazolid-4-one (IX; R = H) [26] were prepared and their infrared spectra compared with that of our product. For the acid there was some masking in the vital region, but for the compound (IX; R = H) and our product the CO·NH frequencies were identical (1670 $cm.^{-1}$), proving that the five-membered ring structure (VII) is correct.

It is difficult to find a satisfactory mechanism for the formation of this product. It

[21] (*a*) Sprague and Land in Elderfield's "Heterocyclic Compounds," John Wiley and Sons, New York, 1957, Vol. V, pp. 484 *et seq.*; (*b*) Wiley, England, and Behr, *Org. Reactions*, 1955, **6**, 367.
[22] Marrian, *J.*, 1949, 1515.
[23] Marrian, *J.*, 1949, 1797.
[24] Cf. Gregory, *J. Amer. Chem. Soc.*, 1955, **77**, 3922.
[25] Andreasch, *Monatsh.*, 1895, **16**, 789; 1897, **18**, 56.
[26] Andreasch, *Monatsh.*, 1887, **8**, 407.

was formed, not only in aqueous alcohol (Marrian) and in aqueous buffers, but also in absolute alcohol. This rules out the possibility of the opening of the maleimide ring by addition of the elements of water, and subsequent elimination of water by a reaction involving the amino-group of thiourea. Two reactions would seem to be necessary: addition of the thiol form of thiourea across the double bond of the maleimide followed by nucleophilic attack by the more basic thiourea amino-group on the adjacent carbonyl group, with subsequent proton shift, as shown in the formulæ.

*Experimental.*—The general experimental conditions adopted were those described in Part I.

We are greatly indebted to Dr. N. Sheppard for his assistance in determining and interpreting the infrared spectra. One of us (J. R. B.) thanks the Department of Scientific and Industrial Research for a maintenance grant.

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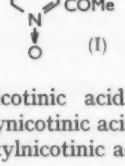
## 1031. *The Reaction of Nicotinic Acid* 1-*Oxide and* 3-*Picoline* 1-*Oxide with Acetic Anhydride.**

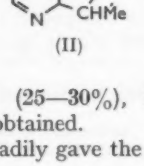
By B. M. BAIN and J. E. SAXTON.

Nicotinic acid 1-oxide reacts with acetic anhydride to give as principal product 2-acetylnicotinic acid 1-oxide; 2-hydroxynicotinic acid and 6-hydroxynicotinic acid are by-products. Nicotinic acid 1-oxide and propionic anhydride give a neutral diketone (III), together with 2- and 6-hydroxynicotinic acid; 2-propionylnicotinic acid 1-oxide is formed when reaction times are very short. Isonicotinic acid 1-oxide and cinchomeronic acid 1-oxide are deoxygenated by acetic anhydride. 3-Picoline 1-oxide and acetic anhydride give 3-methyl-2-pyridone, 5-methyl-2-pyridone, and 3-methyl-1-(5-methyl-2-pyridyl)-2-pyridone. Under the same conditions 3-hydroxypyridine 1-oxide gives 2,3-dihydroxypyridine as the only product isolated. The mechanisms of these reactions are briefly discussed.

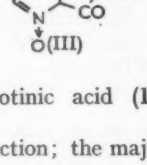
ALTHOUGH the rearrangements of pyridine *N*-oxides have been studied extensively in recent years, there appears to be no record of the behaviour of nicotinic acid 1-oxide towards acetic anhydride. The available evidence relating to the rearrangements of 3-substituted pyridine *N*-oxides (*e.g.*, the reaction of nicotinic acid 1-oxide with phosphorus pentachloride and phosphorus oxychloride,[1] and the reaction of 3-picoline 1-oxide with acetic anhydride [2]) led us, *ab initio*, to expect a preponderance of 2-hydroxynicotinic acid in the product. When nicotinic acid 1-oxide was boiled with acetic anhydride for six hours



(I)



(II)



(III)

2-acetylnicotinic acid 1-oxide (I) (25—30%), 2-hydroxynicotinic acid (10%), and 6-hydroxynicotinic acid (3%) were obtained.

2-Acetylnicotinic acid 1-oxide readily gave the haloform reaction; the major product

* A preliminary account of part of this work has been reported in *Chem. and Ind.*, 1960, 402.

[1] Taylor and Crovetti, *J. Org. Chem.*, 1954, **19**, 1636.
[2] Boekelheide and Linn, *J. Amer. Chem. Soc.*, 1954, **76**, 1286.

was identified as quinolinic acid 1-oxide, which was also prepared by the peracetic acid oxidation of quinolinic acid at room temperature. The *N*-oxide function in (I) was smoothly removed by catalytic hydrogenation, and the product, 2-acetylnicotinic acid, was characterised as the known oxime anhydride [3] and *p*-nitrophenylhydrazone anhydride.[4] When hydrogenation proceeded until 2 moles of hydrogen had been absorbed, the product isolated after sublimation of the crude material was the lactone (II) of 2-1′-hydroxyethylnicotinic acid.

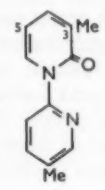
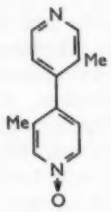
None of the other carboxylic acid *N*-oxides in this series underwent acetylation when heated with acetic anhydride. Isonicotinic acid 1-oxide suffered mainly deoxygenation, but a small yield of 2-hydroxyisonicotinic acid was isolated, together with a substance, $C_9H_9NO_4$, of unknown constitution. Cinchomeronic acid 1-oxide was also deoxygenated under similar conditions. Picolinic acid 1-oxide was readily decarboxylated, hence the products of reaction with acetic anhydride were the same as those obtained from pyridine 1-oxide.[5,6] Similarly, quinolinic acid 1-oxide gave the same products as nicotinic acid 1-oxide.

In an attempt to widen the scope of this reaction we investigated the behaviour of nicotinic acid 1-oxide with propionic anhydride. Under conditions similar to those adopted with acetic anhydride (140° for 4—6 hours) there was no reaction, nicotinic acid 1-oxide being insoluble in propionic anhydride at this temperature. When the mixture was boiled for 3 hours, the acidic products were 2- and 6-hydroxynicotinic acid, but we failed to isolate the expected keto-acid. Instead, we obtained a neutral ketone which we formulate tentatively as (III). When shorter reaction times were used (1 hour at the boiling point), we obtained a non-crystalline, non-acidic fraction which exhibited bands at 1802 and 1764 cm.$^{-1}$ in the infrared spectrum, characteristic of an anhydride grouping. Since the propionic anhydride had been removed at 120°/12 mm. it is probable that this oil consists of anhydrides of nicotinic acid derivatives, contaminated with traces of propionic anhydride. After hydrolysis with water at 100°, the resulting crystalline mixture was separated into 2-propionylnicotinic acid 1-oxide (5%) and 2-hydroxynicotinic acid. The acidic fraction from this reaction contained small amounts of 2- and 6-hydroxynicotinic acid. Since no neutral ketone was isolated under these conditions, whereas ketone but no keto-acid was isolated when using longer reaction times, it seems probable that the initial product of reaction is the keto-acid, which then suffers cyclodehydration to the diketone (III).

The isolation of the ketones (I) and (III) prompted us to investigate the reactions of other 3-substituted pyridine 1-oxides with acetic anhydride, with particular reference to the possibility of ketone formation. In an earlier study with 3-picoline 1-oxide, Boekelheide and Linn [2] obtained a moderate yield of 2-acetoxy-3-methylpyridine, but they did not account for the remainder of their material. In our experiments with 3-picoline 1-oxide, the crude product was hydrolysed with water, and then chromatographed on neutral alumina. The following products were thus obtained, in order of elution: 3-methyl-1-(5-methyl-2-pyridyl)-2-pyridone (IV) (4%), 3-methyl-2-pyridone (35—40%), and 5-methyl-2-pyridone (35—40%). Neither the crude product nor any of the eluates gave evidence of containing ketonic material, and we believe that if any ketones are formed, they are only present in the product in minimal yield. The infrared spectrum of the minor product (IV) exhibits twin absorption bands at 1277 and 1267 cm.$^{-1}$, which almost coincide with the *N*-oxide bands at 1282 and 1272 cm.$^{-1}$ in the spectrum of 3-picoline 1-oxide. However, this substance did not contain an *N*-oxide function, since it was not hydrogenated under conditions which smoothly reduced the *N*-oxide grouping in 2-acetylnicotinic acid 1-oxide, and it was also stable to nascent hydrogen (iron–acetic acid) under conditions which quantitatively removed the oxygen

[3] Rosenheim and Tafel, *Ber.*, 1893, **26**, 1501.
[4] Wibaut and Boer, *Rec. Trav. chim.*, 1955, **74**, 241.
[5] Boekelheide and Lehn, *J. Org. Chem.*, 1961, **26**, 428.
[6] Sauermilch, *Arch. Pharm.*, 1960, **293**, 452.

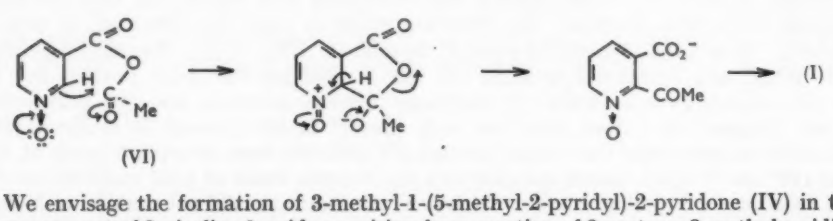
atom from 3,3′-dimethyl-4,4′-bipyridyl 1-oxide (V). The chromophore present in (IV) was inferred from a comparison of its ultraviolet absorption with that of 1-2′-pyridyl-2-pyridone,[7] and its constitution was established by synthesis from the sodium salt of 3-methyl-2-pyridone and 2-bromo-5-methylpyridine. 5-Methyl-1-(5-methyl-2-pyridyl)-2-pyridone was also synthesised for reference purposes; we have not observed its formation in the reaction of 3-picoline 1-oxide with acetic anhydride.

(IV)   (V)

Finally, we have also examined the rearrangement of 3-hydroxypyridine 1-oxide with acetic anhydride, which gave a moderate yield of 2,3-dihydroxypyridine. We have not found any evidence for the formation of 2,5-dihydroxypyridine or of any ketones in this reaction, which affords a convenient alternative preparation of 2,3-dihydroxypyridine to the one hitherto available.[8]

The direct introduction of an acyl group into the pyridine *N*-oxide nucleus by what is in effect an electrophilic substitution is at present unique. However, the detailed mechanism of the formation of the *N*-oxide (I) is still obscure; it presumably cannot proceed by a Fries-type rearrangement of the 1-acetoxy-3-carboxypyridinium ion for obvious electronic reasons. Also, if such a mechanism operated, we should expect 3-hydroxypyridine 1-oxide to undergo acylation with acetic anhydride, and, indeed to react more readily than nicotinic acid 1-oxide. In addition, neither nicotinic acid 1-oxide nor 3-picoline 1-oxide could be acylated by the Friedel–Crafts reaction; pyridine 1-oxide and 3-methoxypyridine 1-oxide have also been reported to be unreactive.[9]

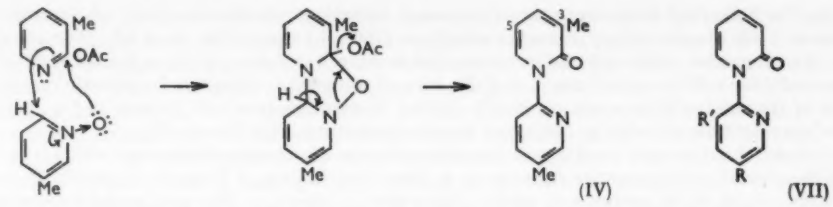
Although the reactions between pyridine *N*-oxides and acetic anhydride frequently show the typical characteristics of free-radical reactions,[10] we do not consider that the formation of the keto-acid (I) can be satisfactorily explained by a free-radical mechanism. It is evident that the keto-acid (I) is formed by a specific process which does not allow the participation of ethyl nicotinate 1-oxide,[5] isonicotinic acid 1-oxide, 3-picoline 1-oxide, or 3-hydroxypyridine 1-oxide. A more likely possibility seems to be intramolecular rearrangement of the mixed anhydride (VI), *via* a cyclic transition state:



(VI)

We envisage the formation of 3-methyl-1-(5-methyl-2-pyridyl)-2-pyridone (IV) in the rearrangement of 3-picoline 1-oxide as arising from reaction of 2-acetoxy-3-methylpyridine with unchanged 3-picoline 1-oxide:

[7] de Villiers and den Hertog, *Rec. Trav. chim.*, 1957, **76**, 647.
[8] Kudernatsch, *Monatsh.*, 1897, **18**, 617.
[9] Mosher and Welch, *J. Amer. Chem. Soc.*, 1955, **77**, 2902.
[10] Boekelheide and Harrington, *Chem. and Ind.*, 1955, 1423; Traynelis and Martello, *J. Amer. Chem. Soc.*, 1958, **80**, 6590; 1960, **82**, 2744.



(IV) (VII)

This possibility is supported by the reaction of 3-picoline 1-oxide with 2-acetoxypyridine at 100°, from which we isolated small yields of 1-(5-methyl-2-pyridyl)-2-pyridone (VII; R = Me, R′ = H), 1-(3-methyl-2-pyridyl)-2-pyridone (VII; R = H, R′ = Me), and 2-pyridone (considerable yields of starting materials were recovered). Clearly the presence of acetic anhydride is not an essential prerequisite for the formation of (VII) or, presumably, of (IV).

The mechanism outlined above involves an initial nucleophilic attack at position 2 in a 2-substituted pyridine by an *N*-oxide function, followed by internuclear transfer of the *N*-oxide oxygen atom. It was first suggested to account for the formation of 1-(5-methyl-2-pyridyl)-2-pyridone (VII; R = Me, R′ = H) in the reaction of 2-bromopyridine with 3-picoline 1-oxide.[11] In the present context internuclear transfer of oxygen cannot readily be demonstrated, and at least one other mechanism can be written which does not involve such a transfer. However, we believe that the analogy is sufficiently close to allow the same mechanism to operate in the reaction of 3-picoline 1-oxide with 2-acetoxypyridine, and in the reaction of 3-picoline 1-oxide with acetic anhydride. The isolation from the former reaction of 1-(3-methyl-2-pyridyl)-2-pyridone (VII; R = H, R′ = Me) is of interest; it indicates that the steric factors invoked by Ramirez and von Ostwalden[11] to account for the non-formation of this substance in the reaction between 3-picoline 1-oxide and 2-bromopyridine are not decisive.

## Experimental

*Reaction of Nicotinic Acid* 1-*Oxide with Acetic Anhydride.*—(*a*) A solution of nicotinic acid 1-oxide (15 g.) in acetic anhydride (150 ml.) was boiled for 6 hr. The solvent was then removed, under reduced pressure, dilute potassium hydroxide solution (90 ml.) was added, and the mixture was heated on the steam-bath for 15 min. An excess of concentrated hydrochloric acid was added. The dark crystalline product was recrystallised from water (charcoal), ethanol, and finally from water. 2-*Acetylnicotinic acid* 1-*oxide* (5·3 g., 27%) was obtained as colourless rhombs, m. p. 247—248° (decomp.), with previous darkening above 230°; $\lambda_{max.}$ (in water) 214·5 and 261 mμ (log ε 4·30 and 3·98); inflexion at 310 mμ (log ε 2·76); ν 1754, 1730, 1242, 784, and 772 cm.$^{-1}$ (potassium chloride disc) (Found: C, 52·95; H, 3·9; N, 7·7. $C_8H_7NO_4$ requires C, 53·05; H, 3·9; N, 7·7%). The acidified mother liquors from the reaction mixture were evaporated to dryness, the residue was extracted repeatedly with boiling ethanol, and the combined extracts were concentrated to crystallisation point. When crystallisation was complete, the dark solid was collected, and crystallised thrice from water (charcoal). The product thus obtained was a mixture of short, dense prisms and fine needles, from which the latter were separated by preferential solution in hot water, followed by decantation. The cooled solution deposited 2-hydroxynicotinic acid, which was recrystallised from water, and obtained as fine needles (1·5 g., 10%), m. p. and mixed m. p. with authentic 2-hydroxynicotinic acid, 260—262° (Found: C, 51·95; H, 3·6; N, 10·1. Calc. for $C_6H_5NO_3$: C, 51·8; H, 3·6; N, 10·1%). Recrystallisation of the short, dense prisms from aqueous acetic acid (1 : 1) gave 6-hydroxynicotinic acid (0·6 g., 3%) as dense, pale brown prisms, m. p. and mixed m. p. with authentic 6-hydroxynicotinic acid, 318—320° (decomp.) with previous darkening >300°. The infrared spectra of 2- and 6-hydroxynicotinic acid thus obtained were identical with those of authentic specimens.

[11] Ramirez and von Ostwalden, *Chem. and Ind.*, 1957, 46; *J. Amer. Chem. Soc.*, 1959, **81**, 156.

(*b*) The following is one example of the many variations which were tried. A solution of nicotinic acid 1-oxide (15 g.) in acetic anhydride (150 ml.) was boiled for 6 hr. The solvent was then removed under reduced pressure, the residue was taken up in methanol (120 ml.) (charcoal), the solution was filtered, and the solvent removed. Repeated fractional crystallisation of the residue from water eventually yielded 2-acetylnicotinic acid 1-oxide (5·0 g., 25%), 2-hydroxynicotinic acid (1·2 g., 8%), and 6-hydroxynicotinic acid (0·4 g., 2%).

2-Acetylnicotinic acid 1-oxide was characterised as its *dinitrophenylhydrazone*, which crystallised from acetic acid as orange rhombs, m. p. 244—245° (decomp.) (Found: C, 46·45; H, 3·2; N, 19·2. $C_{14}H_{11}N_5O_7$ requires C, 46·55; H, 3·05; N, 19·4%). The p-*nitrophenylhydrazone anhydride* was obtained from acetic acid as buff needles, m. p. 266—267° (decomp.) [Found: C, 54·9; H, 4·1; N, 17·1. $C_{14}H_{10}N_4O_4$,0·5AcOH requires C, 54·9; H, 3·7; N, 17·1. Found (after being dried at 116° *in vacuo*): C, 56·6; H, 3·45; N, 18·85. $C_{14}H_{10}N_4O_4$ requires C, 56·4; H, 3·4; N, 18·8%].

*Quinolinic Acid 1-Oxide.*—(*a*) An ice-cold solution of bromine (1·45 g.) in dilute sodium hydroxide solution (1·1 g. in 10 ml. of water) was added to a solution of 2-acetylnicotinic acid 1-oxide (540 mg.) in dilute sodium hydroxide solution (2N; 5 ml.), with cooling in ice. Almost immediately bromoform began to separate. After 1 hr. at 0°, and 4 hr. at room temperature, the mixture was extracted with ether, and the aqueous layer was acidified (Congo Red) with concentrated hydrochloric acid and kept at 0° overnight. The product was then recrystallised from water. *Quinolinic acid 1-oxide* (430 mg., 80%) was thus obtained as rhombs, m. p. 260—262° (decomp.), alone or in admixture with authentic quinolinic acid 1-oxide (Found: C, 46·05; H, 2·7; N, 7·8. $C_7H_5NO_5$ requires C, 45·9; H, 2·7; N, 7·65%). The infrared spectra of this compound and of quinolinic acid 1-oxide, prepared as described below, were identical.

(*b*) A mixture of quinolinic acid (5 g.), acetic acid (25 ml.), and 40% hydrogen peroxide (25 ml.) was warmed *gently* on the steam-bath until solution was complete, and then kept at room temperature overnight. The solid (quinolinic acid) which separated was removed and the mother liquors were kept at room temperature for 7 days. The solid was then recrystallised from water; quinolinic acid 1-oxide (2·5 g., 50%) was obtained as rhombs, m. p. 260—261° (decomp.) (Found: C, 45·95; H, 2·75; N, 7·7%).

*Cinchomeronic Acid 1-Oxide.*—A mixture of cinchomeronic acid (5 g.), acetic acid (15 ml.), and 40% hydrogen peroxide (15 ml.) was heated on the steam-bath for 5 hr. The solvent was then removed under reduced pressure, and the residue was crystallised from water. *Cinchomeronic acid 1-oxide* (2·6 g., 47%) was thus obtained as rhombs, m. p. 249—250° (decomp.) (Found: C, 46·1; H, 2·75; N, 7·6%). The m. p. of a mixture with cinchomeronic acid was 230—244°.

*2-Acetylnicotinic Acid.*—A solution of 2-acetylnicotinic acid 1-oxide (2 g.) in water (60 ml.) was hydrogenated at atmospheric pressure, 5% palladised charcoal catalyst (0·2 g.) being used, until one mole of hydrogen had been absorbed. The catalyst was then removed, the solution evaporated to dryness, and the residue sublimed at 100°/0·03 mm. The sublimate was recrystallised twice from benzene, and 2-acetylnicotinic acid was obtained as needles, m. p. 127—128°; ν 1754, 1710sh, and 789 cm.$^{-1}$ (potassium chloride disc) [Found (after being dried at 78° *in vacuo*): C, 58·1; H, 4·1; N, 8·6. Calc. for $C_8H_7NO_3$: C, 58·2; H, 4·3; N, 8·5%]; Rosenheim and Tafel [3] report m. p. 127°. The oxime anhydride was obtained from ethanol as long needles, m. p. 165—166° (Found: C, 59·55; H, 3·6. Calc. for $C_8H_6N_2O_2$: C, 59·3; H, 3·7%); Rosenheim and Tafel [3] give m. p. 171°. The *p*-nitrophenylhydrazone anhydride crystallised from benzene as pale yellow needles, m. p. 268° (Found: C, 59·35; H, 3·35; N, 19·95. Calc. for $C_{14}H_{10}N_4O_3$: C, 59·6; H, 3·55; N, 19·85%); Wibaut and Boer [4] give m. p. 270°.

*Lactone of 2-1′-Hydroxyethylnicotinic Acid.*—A solution of 2-acetylnicotinic acid 1-oxide (1·00 g.) in water (30 ml.) was hydrogenated at atmospheric pressure in the presence of 5% palladised charcoal catalyst. When 2 moles of hydrogen had been absorbed the solution was filtered and evaporated to dryness. The reddish-brown semisolid residue (0·8 g.) was sublimed at 110°/0·03 mm. The sublimate was dissolved in boiling benzene (charcoal), the solvent was removed, and the residue was crystallised twice from cyclohexane. The *lactone* (II) of 2-1′-hydroxyethylnicotinic acid (0·38 g.) was obtained as needles, m. p. 77·5—79°; $\lambda_{max.}$ (in ethanol) 270 mμ (log ε 3·71); ν 1767 cm.$^{-1}$ (potassium chloride disc) (Found: C, 64·4; H, 4·75; N, 9·4. $C_8H_7NO_2$ requires C, 64·4; H, 4·73; N, 9·4%).

*Reaction of Nicotinic Acid 1-Oxide with Propionic Anhydride.*—(*a*) A solution of nicotinic acid 1-oxide (20 g.) in propionic anhydride (200 ml.) was boiled for 3 hr. The solvent was then

removed under reduced pressure, the residue was dissolved in water (400 ml.), and the aqueous solution was extracted with chloroform. The aqueous layer was concentrated until crystallisation began. The solid was fractionally crystallised from water (charcoal), yielding 2-hydroxynicotinic acid (3·6 g.), m. p. and mixed m. p. with authentic material 260—262°, and 6-hydroxynicotinic acid (0·4 g.), m. p. and mixed m. p. with authentic material 318° (decomp.). The chloroform extract was washed with dilute sodium carbonate solution, dried ($MgSO_4$), and evaporated. The crude product was recrystallised repeatedly from ethanol, and the *diketone* (III) (2·0 g.) was obtained as long cream needles, m. p. 160—161°; $\lambda_{max.}$ (in water) 288 (log ε 3·95) and 335 mμ (log ε 3·49); ν 1727, 1670, 1250sh, 1242, and 787 cm.$^{-1}$ (potassium chloride disc) (Found: C, 61·1; H, 4·1; N, 8·2. $C_9H_7NO_3$ requires C, 61·0; H, 3·95; N, 7·9%). This diketone gave an intense green colour with ferric chloride but was insoluble in dilute sodium carbonate solution. With dilute sodium hydroxide solution it gave an orange-red solid, which dissolved when warmed to give a red solution, the colour of which gradually faded to orange. The *dinitrophenylhydrazone* crystallised from acetic acid as orange-brown needles, m. p. 271—272° (decomp.) (Found: C, 50·45; H, 3·4; N, 19·5. $C_{15}H_{11}N_5O_6$ requires C, 50·4; H, 3·1; N, 19·6%).

(*b*) A mixture of nicotinic acid 1-oxide (6 g.) and propionic anhydride (90 ml.) was boiled for 1 hr., and the solvent was removed at 120°/12 mm. The black tarry residue was extracted with chloroform, and the extracts were washed several times with dilute sodium carbonate solution and then with water. The chloroform solution was then dried ($MgSO_4$) and evaporated, yielding a viscous brown oil which exhibited infrared bands at 1802s, 1764s, 1724 infl., and 1664m cm.$^{-1}$. A mixture of this oil and water (100 ml.) was boiled for 2 hr., then treated with charcoal, filtered, and evaporated to dryness. The residue (3·2 g.) crystallised completely on trituration with methylene chloride, and was recrystallised from the same solvent. The product was repeatedly recrystallised from water, yielding 2-*propionylnicotinic acid* 1-*oxide* (5%) as long prisms, m. p. 195—196° (Found: C, 55·4; H, 4·75; N, 7·45. $C_9H_9NO_4$ requires C, 55·4; H, 4·6; N, 7·2%); $\lambda_{max.}$ (in water) 214 and 261 mμ (log ε 4·33 and 3·99), inflexion at 310 mμ (log ε 2·86). The dinitrophenylhydrazone was prepared in ethanol but was amorphous. The methylene chloride mother liquors were evaporated to dryness and the residue was fractionally crystallised from water, yielding 2-hydroxynicotinic acid, m. p. 260—262° (5%), identical (mixed m. p. and infrared spectrum) with authentic material.

In another experiment the mixture was evaporated to dryness and the residue was extracted with boiling water (total volume 150 ml.). The cooled solution was extracted with chloroform, and the aqueous layer was evaporated to dryness. Fractional crystallisation of the residue from water gave small amounts of 2-hydroxynicotinic acid and 6-hydroxynicotinic acid.

*Reaction of Isonicotinic Acid* 1-*Oxide with Acetic Anhydride.*—A mixture of isonicotinic acid 1-oxide (20 g.) and acetic anhydride (200 ml.) was boiled for 8 hr., then filtered, and the dark brown residue was crystallised repeatedly from water (charcoal). Isonicotinic acid (3·9 g.) was obtained as needles, which darken above 240° and sublime at 310°. The infrared spectrum of this material was identical with that of authentic isonicotinic acid. The acetic anhydride mother liquor was evaporated to dryness under reduced pressure, and the dark residue (7 g.) fractionally crystallised from water (charcoal). The major product was 2-hydroxyisonicotinic acid (1·4 g.) which was obtained as pale yellow-brown needles, which darken above 270° but do not melt below 330° (Found: C, 51·55; H, 3·4; N, 9·65. Calc. for $C_6H_5NO_3$: C, 51·8; H, 3·6; N, 10·05%); Baümler, Sorkin, and Erlenmeyer [12] report m. p. 318—325° (decomp.). The less soluble fractions gave a *substance* $C_9H_9NO_4$ (0·15 g.), obtained as long, colourless needles, m. p. 204—206° (Found: C, 55·4; H, 4·8; N, 7·25. $C_9H_9NO_4$ requires C, 55·4; H, 4·6; N, 7·2%).

*Reaction of Cinchomeronic Acid* 1-*Oxide with Acetic Anhydride.*—A mixture of cinchomeronic acid 1-oxide (2 g.) and acetic anhydride (20 ml.) was boiled for 2 hr., and the solvent was then removed. The residue was dissolved in water (charcoal), and the solution was filtered and evaporated to dryness. The residue was recrystallised from water, and cinchomeronic acid (1 g.) was obtained as long prisms, m. p. 266—267°, alone or when mixed with authentic cinchomeronic acid. The infrared spectra of the two specimens were identical.

*Reaction of* 3-*Picoline* 1-*Oxide with Acetic Anhydride.*—A solution of 3-picoline 1-oxide (5 g.) in acetic anhydride (25 ml.) was boiled for 5 hr., and the solvent was removed under

[12] Bäumler, Sorkin, and Erlenmeyer, *Helv. Chim. Acta*, 1951, **34**, 496.

reduced pressure. Water (25 ml.) was then added, and the mixture was heated on the steam-bath for 1 hr. The solution was then evaporated to dryness under reduced pressure, and the residue (5·5 g.) dissolved in light petroleum (b. p. 60—80°) and chromatographed on neutral alumina (200 g.). Elution with light petroleum (b. p. 60—80°) containing benzene (10%) gave *3-methyl-1-(5-methyl-2-pyridyl)-2-pyridone*, which was obtained from light petroleum (b. p. 60—80°) as plates, m. p. 110—111° (0·18 g., 3·9%); $\lambda_{max.}$ (in water) 264·5, 270, and 303 mμ (log ε 3·7, 3·71, and 3·84); ν 1656, 1613, 1277, and 1267 cm.$^{-1}$ (potassium chloride disc) (Found: C, 72·1; H, 6·1; N, 14·45. $C_{12}H_{12}N_2O$ requires C, 72·0; H, 6·0; N, 14·0%). Elution with light petroleum (b. p. 60—80°)–benzene (3 : 1) furnished 3-methyl-2-pyridone (1·65 g.), m. p. 142—143°, identical (mixed m. p. and infrared spectrum) with authentic material, followed by a mixture (1·53 g.) of 3-methyl- and 5-methyl-2-pyridone. Elution with benzene and with benzene–chloroform then gave 5-methyl-2-pyridone (1·23 g.), m. p. 184—185°, identical (mixed m. p. and infrared spectrum) with authentic material. Rechromatography of the intermediate mixed fraction on neutral alumina (60 g.) yielded more 3-methyl- (0·5 g.) and 5-methyl-2-pyridone (0·3 g.).

*3-Methyl-1-(5-methyl-2-pyridyl)-2-pyridone.*—A mixture of the sodium salt of 3-methyl-2-pyridone (3·22 g.), 2-bromo-5-methylpyridine (4·65 g.), and copper bronze (0·1 g.) was heated at 165° for 5 hr. The cooled mixture was extracted with chloroform, and the extracts were filtered, dried, and concentrated. The residue was recrystallised from light petroleum (b. p. 60—80°) (charcoal); 3-methyl-1-(5-methyl-2-pyridyl)-2-pyridone (2·5 g.) was then obtained as needles, m. p. 110—111°, identical (mixed m. p. and infrared spectrum) with the by-product obtained in the reaction of 3-picoline 1-oxide with acetic anhydride (Found: C, 71·75; H, 5·85; N, 13·95. $C_{12}H_{12}N_2O$ requires C, 72·0; H, 6·0; N, 14·0%).

*5-Methyl-1-(5-methyl-2-pyridyl)-2-pyridone.*—The procedure of the preceding experiment was repeated with the sodium salt of 5-methyl-2-pyridone (1·55 g.), 2-bromo-5-methylpyridine (2·74 g.), and copper bronze (0·1 g.). *5-Methyl-1-(5-methyl-2-pyridyl)-2-pyridone* (1·0 g.) was obtained as needles, m. p. 102—103°; $\lambda_{max.}$ (in water) 264, 269, and 313 mμ (log ε 3·62, 3·60, and 3·78); ν 1675, 1626, 1613, 1287, and 1266 cm.$^{-1}$ (potassium chloride disc) (Found: C, 72·1; H, 6·15; N, 14·05%). The m. p. of a mixture with the product, m. p. 110—111°, obtained from the reaction of 3-picoline 1-oxide was 85—100°.

*3,3′-Dimethyl-4,4′-bipyridyl 1-Oxide.*—3,3′-Dimethyl-4,4′-bipyridyl [13] (0·4 g.) was added to a solution of perbenzoic acid (0·3 g.) in chloroform (30 ml.), and the solution kept overnight. It was then extracted with dilute sodium carbonate solution, dried, and evaporated, and the residue recrystallised from benzene (charcoal). *3,3′-Dimethyl-4,4′-bipyridyl 1-oxide* (0·3 g.) was obtained as rhombs, m. p. 217—218°; $\lambda_{max.}$ (in water) 263 mμ (log ε 4·30); ν 1616, 1253, 1030, 1018, 872, and 830 cm.$^{-1}$ (potassium chloride disc) (Found: C, 72·25; H, 6·0; N, 14·5%). When a mixture with iron powder and acetic acid was boiled for 1·5 hr. smooth, quantitative reduction took place to 3,3′-dimethyl-4,4′-bipyridyl, m. p. 122—123°, identified by mixed m. p. and infrared spectrum.

*2,3-Dihydroxypyridine.*—(*a*) A solution of 3-hydroxypyridine 1-oxide (1·1 g.) in acetic anhydride (10 ml.) was boiled for 4 hr., and the solvent was removed. Water (25 ml.) was then added, and the mixture boiled (charcoal) and filtered. When cold, the solution was filtered to remove tar, and then evaporated to dryness. The residue was recrystallised from water, and 2,3-dihydroxypyridine was obtained as needles, m. p. 252—253°, with previous darkening above 215°, identical (mixed m. p. and infrared spectrum) with authentic 2,3-dihydroxypyridine; [8] the infrared spectrum had bands at 3150—3080, 1669, 781, and 753 cm.$^{-1}$ (Found: C, 54·1; H, 4·55; N, 12·5. Calc. for $C_5H_5NO_2$: C, 54·1; H, 4·5; N, 12·6%).

(*b*) A mixture of 3-hydroxypyridine (5 g.), acetic acid (40 ml.), and 40% hydrogen peroxide (30 ml.) was heated for 18 hr. on the steam-bath. The solvents were removed under reduced pressure, acetic anhydride (10 ml.) was added, and the solution was evaporated to dryness. Acetic anhydride (50 ml.) was added, and the solution was boiled for 4 hr. The solvent was removed, water (50 ml.) was added, and the mixture was digested on the steam-bath for 0·5 hr. (charcoal), filtered, and evaporated until crystallisation began. The product was recrystallised from methanol; 2,3-dihydroxypyridine (1·2 g.) was obtained as plates, m. p. and mixed m. p. with authentic 2,3-dihydroxypyridine, 252—253°.

*Reaction of 3-Picoline 1-Oxide with 2-Acetoxypyridine.*—A mixture of 3-picoline 1-oxide

[13] Stoehr and Wagner, *J. prakt. Chem.*, 1893, **48**, 1.

(8·75 g.) and 2-acetoxypyridine (11 g.) was heated at 100° for 4 days, with exclusion of atmospheric moisture. The resulting dark brown oil was then distilled, and the fractions (11·5 g.) boiling below 120°/0·7 mm. were discarded. The residue (6·2 g. of dark brown oil) was dissolved in hot water (20 ml.) (charcoal), the solution was filtered, and the solvent removed. The remaining oil was extracted repeatedly with boiling light petroleum (b. p. 60—80°) (total volume 200 ml.). The cooled extracts (mother liquor A) deposited a mixture (0·75 g.) of colourless crystals and a pale yellow oil. Repeated fractional crystallisation of this mixture alternately from hexane and cyclohexane eventually yielded 1-(5-methyl-2-pyridyl)-2-pyridone, as needles, m. p. 93·5—94·5° (0·25 g.); $\lambda_{max.}$ (in ethanol) 272 and 314 mμ (log ε 3·56 and 3·80); identical (mixed m. p. and infrared spectrum) with authentic 1-(5-methyl-2-pyridyl)-2-pyridone [11] (Found: C, 71·05; H, 5·4; N, 14·85. Calc. for $C_{11}H_{10}N_2O$: C, 70·95; H, 5·4; N, 15·05%). The light-petroleum mother liquors (A) were evaporated to dryness, and the residual mixture (2·5 g.) of oil and crystals was extracted twice with cyclohexane (residue B). Fractional crystallisation of the extracted material (0·6 g.) as before yielded more (0·2 g.) 1-(5-methyl-2-pyridyl)-2-pyridone. The remaining residue (B; 1·9 g.) was dissolved in benzene and filtered through neutral alumina (20 g.). The filtered solution (50 ml.) furnished a pale cream solid (0·55 g.), which was separated by fractional crystallisation from cyclohexane into 1-(5-methyl-2-pyridyl)-2-pyridone (0·2 g.) (less soluble fraction) and 1-(3-methyl-2-pyridyl)-2-pyridone (0·05 g.), m. p. 107·5—108·5°, identical (mixed m. p. and infrared spectrum) with authentic material; [11] $\lambda_{max.}$ 263, 268 infl. and 306 mμ (log ε 3·62, 3·60, and 3·76) (Found: C, 71·2; H, 5·45; N, 14·8%).

The benzene eluates (40 ml.) from the alumina yielded a small quantity (0·46 g.) of greenish-yellow oil, from which 2-pyridone, m. p. and mixed m. p., 106—107·5°, was obtained by crystallisation from benzene–hexane (1 : 4).

(*b*) A mixture of 2-acetoxypyridine (11·0 g.) and 3-picoline 1-oxide (8·75 g.) was heated at 100° for 6 days, with exclusion of atmospheric moisture. The resulting oil was then distilled and the fractions boiling below 117°/0·6 mm. were discarded. The residue was extracted with boiling water (charcoal), the solution was filtered, and the solvent was removed under reduced pressure. The residual oil was extracted exhaustively with cyclohexane, and the extracted material (4·44 g.) chromatographed on neutral alumina (250 g.), benzene–cyclohexane (70 : 30) being used as solvent. Elution was carried out with benzene–cyclohexane mixtures, then benzene, and finally benzene–chloroform (70 : 30), which eluted a broad band exhibiting an intense violet fluorescence. The eluates (5 × 250 ml.) furnished mixtures of 1-(5-methyl-2-pyridyl)-2-pyridone and 1-(3-methyl-2-pyridyl)-2-pyridone, which could not be separated conveniently into their components by fractional crystallisation. All five fractions gave two spots on chromatoplate examination, corresponding in $R_F$ value to the two pure components. The mixture to be analysed was added to the chromatoplate in solution in benzene, and development was carried out by using ethyl acetate. 1-(5-Methyl-2-pyridyl)-2-pyridone was located by its intense fluorescence; both constituents were located as deep orange-yellow spots on a pale orange-brown background after spraying with Dragendorff's reagent.

Vapour-phase chromatography at 204° with a silicone column and helium as carrier gas also demonstrated the presence of two constituents, identified by the addition of authentic material to the chromatographed mixtures as 1-(5-methyl-2-pyridyl)-2-pyridone and its 3-methyl isomer. The composition of the mixtures was determined by estimating the areas of the peaks in each chromatogram, from which the estimated total yields were: 1-(5-methyl-2-pyridyl)-2-pyridone (VII; R = Me, R′ = H), 1·52 g. (10%); and 1-(3-methyl-2-pyridyl)-2-pyridone (VII; R = H, R′ = Me), 0·60 g. (4%).

One of us (B. M. B.) is indebted to the D.S.I.R. for a maintenance allowance.

THE UNIVERSITY, LEEDS 2. [*Received, April 24th,* 1961.]

## 1032. *Dehydrogenation with Mercuric Acetate in the Lupane Series. Part II.*[1] *Lupeol and its Derivatives.*

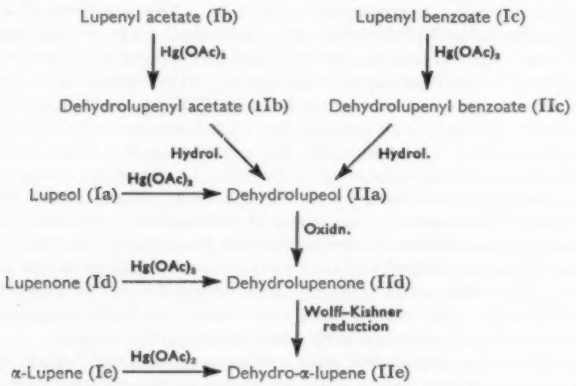
By J. M. Allison, William Lawrie, John McLean, and (in part) J. M. Beaton.

Lupeol, lupenone, α-lupene and lupenyl esters are shown to react with mercuric acetate to give the corresponding dehydro-compounds containing the additional double bond at the 12,13-position.

Dehydrogenation of betulin diacetate and of methyl acetylbetulinate with mercuric acetate results in the formation of 3β,28-diacetoxylupa-12,20(30)-diene and of methyl 3β-acetoxylupa-12,20(30)-diene-28-oate respectively.[1] In the present communication we show that lupeol (Ia), lupenyl acetate (Ib), lupenyl benzoate (Ic), lupenone (Id), and α-lupene (Ie) undergo analogous dehydrogenation at position 12, 13.

The dehydrogenation is effected in all cases in chloroform–acetic acid at room temperature for 14 days or at 100° for 5 hr. Lupenyl acetate (Ib) and lupenyl benzoate (Ic) give the corresponding dehydro-esters (IIb and IIc), each giving on hydrolysis lupa-12,20(30)-dien-3β-ol (IIa). Since the latter is also obtained by dehydrogenation of lupeol (Ia) with mercuric acetate, the same change is occurring with lupeol and its esters during the dehydrogenation.

The dehydrogenation products resulting from lupenone, α-lupene, and lupeol have been interrelated as shown in the scheme. It follows that in the five compounds (Ia—e) the unsaturated linkage is introduced at the same position.




We established the location of this olefinic linkage by reference to the reactions of dehydrolupeol (IIa) and its acetate (IIb).

That the dehydro-compounds (IIa—c) contain two non-conjugated olefinic linkages is evident from ultraviolet absorption and from the reaction of dehydrolupenyl acetate with perbenzoic acid wherein two atoms of oxygen are consumed with formation of 3β-acetoxy-12,13:20,30-diepoxylupane (III), which does not give a colour with tetranitromethane or show selective ultraviolet absorption. This was confirmed when the dehydro-acetate (IIb), on reaction with osmium tetroxide and then lithium aluminium hydride, gave a resinous lupanepentaol (IVa) which afforded a diacetate (IVb); this compound is transparent to ultraviolet light and does not give a colour with tetranitromethane.

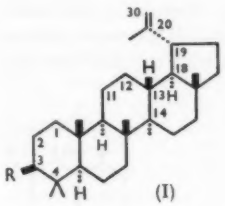
One of the olefinic bonds in the dehydro-compounds is of the vinylidene type showing infrared absorption bands at 1631 and 891 cm.$^{-1}$. Further cleavage of the resinous lupanepentaol with lead tetra-acetate gave formaldehyde. In our previous communication [1] we

[1] Part I, *J.*, 1961, 3353.

showed that rearrangement of the lupene skeleton does not occur during the reaction with mercuric acetate and hence we can assume that the vinylidene group in the dehydro-compounds (IIa—e) occupies the same position as in lupeol.

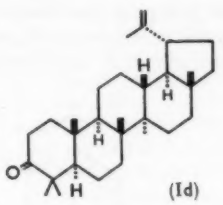
The new double bond which is introduced on dehydrogenation of the lupene derivatives (Ia—e) might be expected to occupy position 12,13 by analogy with the products formed from betulin diacetate and methyl acetylbetulinate,[1] and the evidence which follows confirms this.

Isomerisation of the non-conjugated dienyl acetate (IIb) with hydrochloric acid in acetic acid gave the conjugated diene (Va), $\lambda_{max.}$ 234 mμ (ε 9500) being consistent with a *cisoid* heteroannular diene.[2] A second product was 3β-acetoxylupa-11,13(18)-diene (VIa)

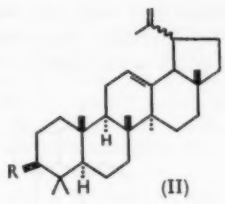


(I)

(a) R = OH; (b) R = OAc
(c) R = OBz; (e) R = H

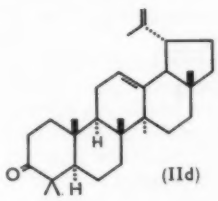


(Id)

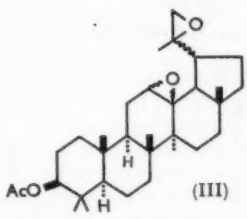


(II)

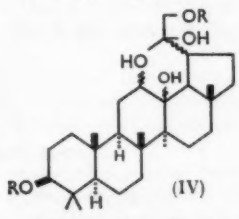
(a) R = OH; (b) R = OAc
(c) R = OBz; (e) R = H



(IId)



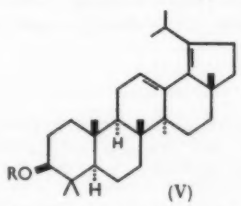
(III)



(IV)

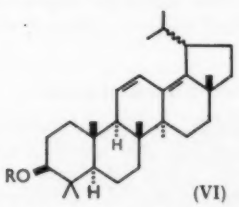
(a) R = H; (b) R = Ac

whose ultraviolet absorption ($\lambda_{max.}$ 244, 252, and 260 mμ, ε 23,000, 27,000, 19,400 respectively) is characteristic of a *transoid* heteroannular diene of type (VI).[2,3] Each of the conjugated dienes (V) and (VI) may be converted into a mixture of both on treatment



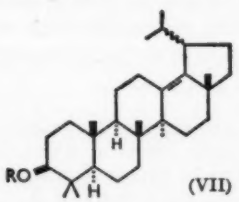
(V)

(a) R = Ac; (b) R = H



(VI)

(a) R = Ac; (b) R = H



(VII)

(a) R = Ac; (b) R = H

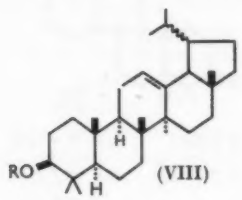
with mineral acid in acetic acid, and hydrogenation of each of the conjugated dienyl acetates (Va) and (VIa) in presence of platinum leads to the fully substituted mono-unsaturated acetate (VIIa), the molecular rotation difference (−1324°) involved in hydrogenation of the *cisoid* dienyl acetate (Va) being in agreement with the increments

[2] Barton and Brooks, *J.*, 1951, 257.
[3] Easton, Manson, and Spring, *J.*, 1953, 943; Beaton, Spring, Stevenson, and Strachan, *J.*, 1955, 2610.

XUM

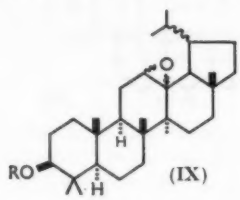
recorded when methyl isodehydro-oleanolate acetate [2] and 3β,28-diacetoxylupa-12,18-diene [1] are hydrogenated (−1410° and −1371° respectively). Also the molecular rotation difference involved in the hydrogenation of the *transoid* dienyl acetate (VIa) (+254°) agrees with the increment recorded (+266°) when ursa-11,13(18)-dienyl acetate is hydrogenated to urs-13(18)-enyl acetate.[3]

The evidence cited above is in keeping with formulæ (IIa—e) for the dehydro-compounds, and additional evidence came from reactions of the dihydro-derivatives (VIII—X) of the dehydrogenation products (II). Hydrogenation of the dehydro-acetate (IIb) in presence of platinum gave 3β-acetoxylup-12-ene (VIIIa), whose ultraviolet absorption ($\lambda_{max.}$ 206 mμ; ε 4000) suggested the presence of a trisubstituted double bond. The olefin (VIIIa) did not absorb in the vinylidene region in the infrared spectrum, thereby showing that only the vinylidene grouping had been reduced. Moreover, the olefin (VIIIa) is readily converted into the saturated epoxylupanyl acetate (IXa) on treatment with either perbenzoic acid or perphthalic acid, and hydroxylation with osmium tetroxide



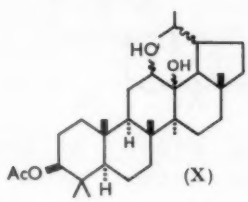

(VIII)

(a) R = Ac; (b) R = H

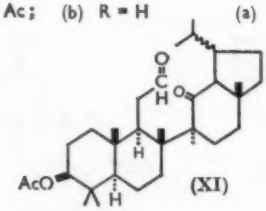



(IX)

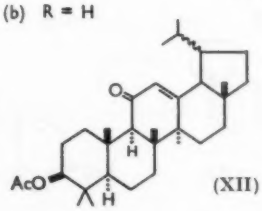
(a) R = Ac; (b) R = H




(X)




(XI)




(XII)

and subsequent acetylation converts it into 3β-acetoxylupane-12,13-diol (X). Lead tetra-acetate cleaves the diol to the keto-aldehyde (XI) whose infrared spectrum (in chloroform) indicates the presence of a keto-aldehyde.

Finally chromic acid oxidised isolupenyl acetate (VIIIa) to the αβ-unsaturated ketone (XII) which on hydrogenation over platinum regenerated isolupenyl acetate. These reactions are characteristic of α- and β-amyrin derivatives [4] in which the double bond is known to be in the 12,13-position.

## Experimental

Rotations were determined for $CHCl_3$ solutions at room temperature, ultraviolet absorption spectra for EtOH solutions (Unicam S.P. 500 spectrophotometer), and infrared spectra for Nujol mulls (unless otherwise stated). Light petroleum refers to the fraction of b. p. 60—80°. Microanalysis were by Dr. A. C. Syme and Mr. W. McCorkindale.

3β-*Acetoxylupa*-12,20(30)-*diene* (IIb).—Lupenyl acetate (10 g.) in chloroform (200 ml.) was treated with mercuric acetate (120 g.) in solution in acetic acid (2 l.) at room temperature for 14 days or at 100° for 5 hr. The mercurous acetate was filtered off, and the filtrate diluted with water and extracted with chloroform. Evaporation of the washed extracts gave an orange solid which was dissolved in pyridine, treated with hydrogen sulphide, and filtered through kieselguhr. Removal of the solvent *in vacuo* gave a solid (8·5 g.) which was dissolved in

[4] Spring and Vickerstaff, *J.*, 1937, 249; Ruzicka, Leuenberger, and Schellenberg, *Helv. Chim. Acta*, 1937, **20**, 1271; Ruzicka, Müller, and Schellenberg, *ibid.*, 1939, **22**, 758; Beynon, Sharples, and Spring, *J.*, 1938, 1233.

benzene–light petroleum (1 : 4) and filtered through alumina (300 g.), to give 3β-*acetoxylupa*-12,20(30)-*diene* (1·7 g.), crystallising from chloroform–methanol as needles, m. p. 229—231°, $[\alpha]_D$ +47° (*c* 1·3), $\lambda_{max.}$ 207 mμ (ε 7000), $\nu_{max.}$ 1736, 1248, 1626, and 891 cm.$^{-1}$ (OAc and vinylidene groups). The compound gave a deep yellow colour with tetranitromethane (Found: C, 82·4; H, 10·9. $C_{32}H_{50}O_2$ requires C, 82·3; H, 10·8%). Treatment of the acetate with lithium aluminium hydride gave *lupa*-12,20(30)-*dien*-3β-*ol* (IIa) which crystallised from chloroform–methanol as needles, m. p. 218—222°, $[\alpha]_D$ +31° (*c* 1·15), $\lambda_{max.}$ 207 mμ (ε 6500), $\nu_{max.}$ 3509 (OH), 1631 and 891 cm.$^{-1}$ (vinylidene) (Found: C, 84·8; H, 11·4. $C_{30}H_{48}O$ requires C, 84·8; H, 11·4%).

The alcohol (IIa) was also obtained by direct dehydrogenation of lupeol with mercuric acetate as described above, the crude product in benzene–ether (9 : 1) being filtered through alumina before crystallisation.

3β-*Benzoyloxylupa*-12,20(30)-*diene* (IIc).—Lupenyl benzoate (17 g.) was treated with mercuric acetate as described above and a solution of the product in benzene–light petroleum (1 : 4) was filtered through alumina (500 g.). Removal of the solvent and crystallisation of the residue from benzene–ethanol gave 3β-*benzoyloxylupa*-12,20(30)-*diene* as rods (3·9 g.), m. p. 280—281°, $[\alpha]_D$ +67·6° (*c* 1·11), $\lambda_{max.}$ 204 and 229 mμ (ε 7400 and 4450, respectively), $\nu_{max.}$ 1733 and 1279 cm.$^{-1}$ (benzoate), and 890 cm.$^{-1}$ (vinylidene) (Found: C, 84·0; H, 10·2. $C_{37}H_{52}O_2$ requires C, 84·0; H, 9·9%). Hydrogenolysis of the benzoate with lithium aluminium hydride gave the alcohol (IIa), identical with the product described above.

*Lupa*-12,20(30)-*dien*-3-*one* (IId).—(a) *Dehydrogenation of lupenone.* Lupenone (4 g.) was treated with mercuric acetate as above, and the product (1·2 g.) eluted from alumina (120 g.) with light petroleum. Removal of solvent and crystallisation from chloroform–methanol gave *lupa*-12,20(30)-*dien*-3-*one* as rods (0·8 g.), m. p. 156—158°, $[\alpha]_D$ +66·3° (*c* 0·93), $\lambda_{max.}$ 207 mμ (ε 7750), $\nu_{max.}$ 1701 (C=O), 1623 and 890 cm.$^{-1}$ (vinylidene). The compound gives a dark yellow colour with tetranitromethane (Found: C, 85·3; H, 11·1. $C_{30}H_{46}O$ requires C, 85·2; H, 11·0%).

(b) *Oxidation of lupa*-12,20(30)-*dien*-3β-*ol* (IIa). A solution of the alcohol (IIa) (0·2 g.) in acetone (15 ml.) was treated dropwise with a 17% solution (1 ml.) of sodium dichromate in 5N-sulphuric acid and set aside for 5 min. Gradual dilution with water then precipitated lupa-12,20(30)-dien-3-one, identical with the product described above.

*Lupa*-12,20(30)-*diene* (IIe).—(a) *Dehydrogenation of* α-*lupene.* α-Lupene (4 g.) was treated with mercuric acetate as in previous cases. The product, eluted from alumina (120 g.) with light petroleum, recrystallised from chloroform–methanol to give *lupa*-12,20(30)-*diene* (0·9 g.), m. p. 160—162°, $[\alpha]_D$ +29·3° (*c* 2·00), $\lambda_{max.}$ 207 mμ (ε 6400), $\nu_{max.}$ 3075, 1626, and 890 cm.$^{-1}$ (vinylidene) (Found: C, 88·4; H, 11·9. $C_{30}H_{48}$ requires C, 88·2; H, 11·8%). The compound depressed the m. p. of α-lupene.

(b) *Reduction of lupa*-12,20(30)-*dien*-3-*one.* The ketone (0·13 g.) in ethanol (5 ml.) was heated in an autoclave with sodium (0·15 g.), ethanol (7 ml.), and 100% hydrazine hydrate (0·5 ml.) at 195° for 6 hr. Isolation of the product in the usual way followed by chromatography on alumina and crystallisation from chloroform–methanol gave lupa-12,20(30)-diene (0·07 g.), m. p. and mixed m. p. 160—162°, $[\alpha]_D$ +30° (*c* 1·42).

3β-*Acetoxy*-12,13:20,30-*diepoxylupane* (III).—A solution of 3β-acetoxylupa-12,20(30)-diene (IIb) (1 g.) in benzene (50 ml.) was treated with 1·9N-perbenzoic acid (10 ml.) at room temperature for 48 hr. The product was isolated by means of benzene and crystallised several times from chloroform–methanol, to give 3β-*acetoxy*-12,13:20,30-*diepoxylupane* as needles (0·44 g.), m. p. 275—277° (*in vacuo*), $[\alpha]_D$ +49° (*c* 0·95), $\nu_{max.}$ 1739 and 1250 cm.$^{-1}$ (OAc). The compound showed no selective absorption in the ultraviolet region and did not give a colour with tetranitromethane (Found: C, 77·0; H, 10·2. $C_{32}H_{50}O_4$ requires C, 77·1; H, 10·1%).

*Hydroxylation of* 3β-*Acetoxylupa*-12,20(30)-*diene* (IIb).—The dienyl acetate (1 g.) in pyridine (10 ml.) was treated with osmium tetroxide (1·6 g.) in ether (20 ml.) and kept in darkness for 11 days. The mixture was diluted with ether (100 ml.), and the osmic ester decomposed by addition of lithium aluminium hydride (4 g.) in ether (50 ml.) during 0·5 hr. followed by 1 hour's refluxing. Isolation of the product through ether gave the crude pentahydroxy-derivative as a gum (0·9 g.) which showed strong absorption at 3300 cm.$^{-1}$ (OH) and only slight end absorption in the ultraviolet region.

*Cleavage of the Pentahydroxy-derivative with Lead Tetra-acetate.*—The pentahydroxy-derivative (0·24 g.) in chloroform (3 ml.) and acetic acid (24 ml.) was treated with lead tetra-acetate

(1 g.) and left for 20 hr. Extraction with water (50 ml.) gave formaldehyde which was isolated as the dimethone (m. p. and mixed m. p. 192°) by addition of a saturated aqueous solution of dimedone to the aqueous extract (Found: C, 69·6; H, 8·0. Calc. for $C_{17}H_{24}O_4$: C, 69·8; H, 8·3%). The reaction mixture was extracted with chloroform after removal of formaldehyde, but material from the chloroform extract did not crystallise.

3β,30-*Diacetoxylupane*-12,13,20-*triol* (IVb).—The pentahydroxy-compound (0·65 g.) in pyridine (5 ml.) was treated with pyridine–acetic anhydride (1 : 1; 30 ml.) at room temperature for 22 hr. Isolation of the product by means of ether followed by chromatography on alumina (25 g.) from benzene–light petroleum (1 : 1; 150 ml.) gave 3β,30-*diacetoxylupane*-12,13,20-*triol* that crystallised from chloroform–light petroleum as plates (0·3 g.), m. p. 239—240° (*in vacuo*), $[\alpha]_D$ +4·6° (*c* 2·64), $\nu_{max.}$ 3484 (OH), 1736, 1712, and 1212 cm.$^{-1}$ (OAc) (Found: C, 70·7; H, 9·8. $C_{34}H_{56}O_7$ requires C, 70·8; H, 9·8%).

*Isomerisation of the Non-conjugated Diene* (IIb) *with Acid*: 3β-*Acetoxylupa*-12,18-*diene*.—3β-Acetoxylupa-12,20(30)-diene (IIb) (2 g.) in acetic acid (200 ml.) at 100° was treated with concentrated hydrochloric acid (5 ml.) and kept at 100° for 15 min. Evaporation of the solvent *in vacuo* and chromatography of the residue on alumina (80 g.) from light petroleum (200 ml.) gave 3β-*acetoxylupa*-12,18-*diene* (Va) (0·72 g.) which crystallised from chloroform–methanol as needles, m. p. 179—181°, $[\alpha]_D$ +260° (*c* 1·43), $\lambda_{max.}$ 234 mμ (ε 9500), $\nu_{max.}$ 1730, 1253, and 1642 cm.$^{-1}$ (OAc and diene) (Found: C, 82·2; H, 11·0. $C_{32}H_{50}O_2$ requires C, 82·3; H, 10·8%). Treatment of the conjugated dienyl acetate (Va) with lithium aluminium hydride in ether and crystallisation of the product from chloroform–methanol gave *lupa*-12,18-*dien*-3β-*ol* (Vb), needles, m. p. 208—211°, $[\alpha]_D$ +82° (*c* 0·82), $\lambda_{max.}$ 234 mμ (ε 8800), $\nu_{max.}$ 3584 and 1639 cm.$^{-1}$ (OH and diene) (Found: C, 84·9; H, 11·7. $C_{30}H_{48}O$ requires C, 84·8; H, 11·4%). Both compounds gave a brown colour with tetranitromethane. After removal of the *cisoid* dienyl acetate (Va) from the column, elution with benzene–light petroleum (1 : 4; 2 l.) and crystallisation from chloroform–methanol gave 3β-*acetoxylupa*-11,13(18)-*diene* (VIa) (0·3 g.), needles, m. p. 155—156°, $[\alpha]_D$ −74·5° (*c* 1·12), $\lambda_{max.}$ 244, 252, 260 mμ (ε 23,000, 27,000, and 19,400), $\nu_{max.}$ 1736, 1245, and 1639 cm.$^{-1}$ (OAc and diene) (Found: C, 82·3; H, 10·9. $C_{32}H_{50}O_2$ requires C, 82·3; H, 10·8%). Treatment of the *transoid* dienyl acetate (VIa) with lithium aluminium hydride in ether and crystallisation of the product from chloroform–methanol gave *lupa*-11,13(18)-*dien*-3β-*ol* (VIb), needles, m. p. 205—207°, $[\alpha]_D$ −80° (*c* 0·66), $\lambda_{max.}$ 242, 250, 260 mμ (ε 21,000, 24,400, and 16,100), $\nu_{max.}$ 3448 and 1639 cm.$^{-1}$ (OH and diene) (Found: C, 84·7; H, 11·7. $C_{30}H_{48}O$ requires C, 84·8; H, 11·4%). Both compounds gave a brown colour with tetranitromethane.

*Equilibration of the Conjugated Dienyl Acetates with Acid*.—(*a*) 3β-Acetoxylupa-12,18-diene (Va) (0·04 g.) in acetic acid (50 ml.) and concentrated hydrochloric acid (1 ml.) was heated at 100° for 1 hr. Removal of solvent followed by chromatography on alumina (3 g.) from light petroleum (10 ml.) gave starting material (0·02 g.) which was identified by m. p., mixed m. p., and infrared and ultraviolet absorption comparison. Continued elution with light petroleum gave a fraction (0·02 g.) which crystallised from methanol to give 3β-acetoxylupa-11,13(18)-diene, needles, m. p. and mixed m. p. 152—154°. The ultraviolet and infrared spectra were identical with those of an authentic sample.

(*b*) 3β-Acetoxylupa-11,13(18)-diene (VIa) (0·08 g.) in acetic acid (50 ml.) and concentrated hydrochloric acid (1 ml.) was heated at 100° for 1 hr. Isolation of the products as in (*a*) gave the *cisoid* dienyl acetate (Va) and the *transoid* dienyl acetate (VIa), which were identified by m. p., mixed m. p., and absorption data.

*Hydrogenation of the Conjugated Dienyl Acetates to give* 3β-*Acetoxylup*-13(18)-*ene* (VIIa).—(*a*) Hydrogenation of 3β-acetoxylupa-12,18-diene (0·12 g.) in acetic acid (100 ml.) containing platinum (from platinum oxide, 100 mg.) for 20 hr. and isolation of the product in the usual manner gave 3β-*acetoxylup*-13(18)-*ene* (0·09 g.), needles (from methanol), m. p. 184—185° (*in vacuo*), $[\alpha]_D$ −20·7° (*c* 1·33), $\lambda_{max.}$ 207 mμ (ε 10,100), $\nu_{max.}$ 1730 and 1241 cm.$^{-1}$ (OAc) (Found: C, 82·2; H, 11·4. $C_{32}H_{52}O_2$ requires C, 82·0; H, 11·2%). The compound gave a yellow colour with tetranitromethane.

(*b*) Hydrogenation of 3β-acetoxylupa-11,13(18)-diene (0·15 g.) as in (*a*) also gave 3β-acetoxylup-13(18)-ene (0·11 g.), m. p. and mixed m. p. 184—185° (*in vacuo*). The infrared and ultraviolet spectra were identical with those of the product obtained as in (*a*). Treatment of the isolupenyl acetate (VIIa) with lithium aluminium hydride in ether and crystallisation of the product from methanol gave *lup*-13(18)-*en*-3β-*ol* (VIIb), m. p. 193—196°, $[\alpha]_D$ −39·4° (*c* 1·22)

$\lambda_{max.}$ 207 mμ (ε 9300), $\nu_{max.}$ 3367 cm.$^{-1}$ (OH) (Found: C, 84·1; H, 11·9. $C_{30}H_{50}O$ requires C, 84·4; H, 11·8%). The compound gives a yellow colour with tetranitromethane.

*Hydrogenation of the Non-conjugated Dienyl Acetate* (IIb).—3β-Acetoxylupa-12,20(30)-diene (1·5 g.) was hydrogenated in ethyl acetate–acetic acid (1 : 1; 600 ml.) over pre-reduced platinum oxide (0·5 g.) for 28 hr. Isolation of the product in the usual manner and crystallisation from chloroform–methanol gave 3β-*acetoxylup*-12-*ene* (VIIIa) as blades (1·2 g.), m. p. 249—251° (*in vacuo*), $[\alpha]_D$ +9° (*c* 1·40), $\lambda_{max.}$ 206 mμ (ε 3600), $\nu_{max.}$ 1739 and 1240 cm.$^{-1}$ (OAc) (Found: C, 81·7; H, 11·2. $C_{32}H_{52}O_2$ requires C, 82·0; H, 11·2%). The compound gave a pale yellow colour with tetranitromethane and on treatment with lithium aluminium hydride in ether, or with 3% alcoholic potassium hydroxide, and crystallisation from methanol gave *lup*-12-*en*-3β-*ol* (VIIIb) as needles, m. p. 225—227° (*in vacuo*), $[\alpha]_D$ −12·5° (*c* 1·21), $\lambda_{max.}$ 206 mμ (ε 6000), $\nu_{max.}$ 3448 cm.$^{-1}$ (OH) (Found: C, 84·2; H, 12·0. $C_{30}H_{50}O$ requires C, 84·4; H, 11·8%).

3β-*Acetoxylup*-12-*en*-11-*one* (XII).—3β-Acetoxylup-12-ene (0·5 g.) in stabilised acetic acid (150 ml.) was treated at room temperature with chromium trioxide (0·2 g.) in 90% acetic acid (70 ml.) for 20 hr. The excess of oxidant was destroyed with methanol, and the product isolated through ether. Chromatography on alumina (20 g.) and elution with light petroleum gave an acetate (0·07 g.), m. p. 272—274°, $[\alpha]_D$ +24° (*c* 1·1), which had no ultraviolet absorption (Found: C, 81·75; H, 11·4%). A second saturated acetate (0·08 g.), m. p. 244—246°, $[\alpha]_D$ +36·5° (*c* 0·7), was eluted with light petroleum–benzene (1:2) (Found: C, 81·6; H, 11·5%). Elution with benzene and benzene–ether (4 : 1) gave fractions which crystallised from chloroform–methanol to yield 3β-*acetoxylup*-12-*en*-11-*one* (XII) as plates (0·26 g.), m. p. 290—292°, $[\alpha]_D$ −61° (*c* 0·9), $\lambda_{max.}$ 244 mμ (ε 13,500), $\nu_{max.}$ 1730, 1235, and 1689 cm.$^{-1}$ (OAc and αβ-unsaturated ketone) (Found: C, 79·8; H, 10·7. $C_{32}H_{50}O_3$ requires C, 79·6; H, 10·4%). The compound gave a faint yellow colour with tetranitromethane. Hydrogenation of the αβ-unsaturated keto-acetate (XII) (0·05 g.) in acetic acid (75 ml.) over pre-reduced platinum oxide (0·04 g.) for 48 hr. and isolation of the product in the usual way gave 3β-acetoxylup-12-ene (VIIIa) (0·04 g.), m. p. and mixed m. p. 248—250° (*in vacuo*), $[\alpha]_D$ +9° (*c* 1·68). The infrared spectrum was identical with that of an authentic specimen.

3β-*Acetoxy*-12,13-*epoxylupane* (IXa).—The acetoxylupene (VIIIa) (0·15 g.) in benzene (5 ml.) was treated with N-perbenzoic acid in benzene (1·5 ml.) at room temperature for 20 hr. The product, isolated in the usual way, was chromatographed in light petroleum (25 ml.) on alumina (15 g.). Light petroleum (200 ml.) eluted a fraction (0·02 g.) which crystallised from methanol as plates, m. p. 226—228°, $[\alpha]_D$ −20·4° (*c* 0·82), $\nu_{max.}$ 1739 and 1242 cm.$^{-1}$ (OAc). The compound did not show selective ultraviolet absorption or give a colour with tetranitromethane (Found: C, 81·5; H, 11·4. $C_{32}H_{52}O_2$ requires C, 82·0; H, 11·2%). Elution with benzene–light petroleum (1 : 3; 1 l.) gave fractions (0·09 g.) which crystallised from methanol, yielding 3β-*acetoxy*-12,13-*epoxylupane* (IXa), blades, m. p. 236—238°, $[\alpha]_D$ +32° (*c* 0·69), $\nu_{max.}$ 1736 and 1242 cm.$^{-1}$ (OAc). The compound did not absorb in the ultraviolet region and did not give a colour with tetranitromethane (Found: C, 79·2; H, 10·7. $C_{32}H_{52}O_3$ requires C, 79·3; H, 10·8%). Treatment of the alcohol (VIIIb) (0·5 g.) with an excess of monoperphthalic acid in ether for 5 days at room temperature and isolation of the product in the usual way gave 12,13-*epoxylupan*-3β-*ol* (IXb) (0·48 g.), needles (from methanol), m. p. 234—236° (*in vacuo*), $[\alpha]_D$ +28·2° (*c* 0·92), $\nu_{max.}$ 3509 cm.$^{-1}$ (OH). The compound did not absorb in the ultraviolet region (Found: C, 81·3; H, 11·6. $C_{30}H_{50}O_2$ requires C, 81·4; H, 11·4%).

3β-*Acetoxylupane*-12,13-*diol* (X).—Osmium tetroxide (0·7 g.) in dry ether (10 ml.) was added to 3β-acetoxylup-12-ene (0·7 g.) in pyridine (5 ml.) and dry ether (10 ml.). The mixture was kept in darkness for 14 days, and the product isolated in the usual manner as a yellow solid (0·62 g.), which was acetylated with pyridine–acetic anhydride at room temperature for 20 hr. Chromatography on alumina (30 g.) from benzene followed by elution with benzene (500 ml.) and benzene–ether (4 : 1; 1500 ml.) gave a product (0·23 g.) which crystallised from chloroform–methanol affording 3β-*acetoxylupane*-12,13-*diol* (X), plates, m. p. 215—245° (decomp.), $[\alpha]_D$ +9° (*c* 0·8), $\nu_{max.}$ 3534 cm.$^{-1}$ (OH), 1712, 1269, and 1255 cm.$^{-1}$ (OAc). The compound did not absorb in the ultraviolet region (Found: C, 76·6; H, 10·8. $C_{32}H_{54}O_4$ requires C, 76·4; H, 10·8%).

3β-*Acetoxy*-12,13-*dioxo*-12,13-*secolupane* (XI).—The triol monoacetate (X) (0·07 g.) in chloroform (10 ml.) and dry benzene (40 ml.) was treated with lead tetra-acetate (0·18 g.) at room temperature for 24 hr., an orange solid separating. The suspension was treated with ethylene glycol (2 drops) and filtered through kieselguhr. Evaporation of the filtrate and

crystallisation of the residue from methanol gave 3β-*acetoxy*-12,13-*dioxo*-12,13-*secolupane* (XI), plates (0·04 g.), m. p. 186—188°, $[\alpha]_D$ +39·5° (*c* 1·05), $\lambda_{max.}$ 280 mμ (ε 150), $\nu_{max.}$ (in $CCl_4$ with a $CaF_2$ prism) 2882, 1717 cm.$^{-1}$ (CHO), 1739, 1240 cm.$^{-1}$ (OAc), 1706 cm.$^{-1}$ (C=O in a six-membered ring) (Found: C, 76·5; H, 10·4. $C_{32}H_{52}O_4$ requires C, 76·75; H, 10·5%).

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## 1033. *Studies on Uronic Acid Materials. Part IV.*[1] *Aqueous Decarboxylation of Uronic Acids, and the Decarboxylation of Pectic Materials during Extraction.*

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Rate-constants for the decarboxylation of some uronic acids in de-ionised water have been determined. The extent of the decarboxylation of pectic materials when heated with (*a*) aqueous 70% ethanol, (*b*) water, (*c*) aqueous ammonium oxalate and (*d*) aqueous ammonium oxalate–oxalic acid has been investigated. The results are discussed with respect to the extraction procedures now used in structural studies; in particular, extraction with ammonium oxalate–oxalic acid solutions at 85—90° should be avoided.

EXTRACTION is an all-important step in structural studies of polysaccharides: fractionation, degradation, chemical modification, and the creation of artefacts[2] are possible consequences of carelessly designed extraction schemes. In initial investigations, one can only use extraction conditions which are, on the basis of previous experience with some similar material, apparently the mildest available, consistent with extraction of the desired polysaccharide in reasonable yield. Poor yields may imply that only a non-representative fraction has been obtained.[3] Preliminary studies establishing an approximation to the composition of a new material may therefore be necessary before the optimum method of extracting a particular component can be devised;[4] even the cation composition can be important.[5] Often, however, as in starch chemistry (cf. ref. 6), less degraded products of higher molecular weight are obtained only after a continued series of studies has refined the method of extraction.

Studies assessing the degradation suffered by the product during extraction should be complementary to structural studies. All too often, structural studies are reported on materials claimed to have been extracted " by the mildest possible means " when, in fact, no experiments were carried out to establish the validity of this statement.

Some polysaccharides, *e.g.*, pectic materials, can at present only be extracted or subsequently purified by methods which degrade and/or chemically modify the material present in the plant. It is then even more important to assess the extent of (*a*) the degradation and (*b*) the modification, such as demethylation and decarboxylation; degradation and chemical modification may be quite independent effects for some polysaccharides. Much is known of the degradation of pectic materials, which can occur in cold alkaline solution,[7,8] buffered (pH 7) " Versene " solution, or, at elevated temperatures, in weakly

[1] Part III, Anderson and Garbutt, *Talanta*, 1961, **8**, 605.
[2] Anderson and King, *Talanta*, 1961, **8**, 497.
[3] Goring and Timell, *J. Phys. Chem.*, 1960, **64**, 1426.
[4] Anderson and King, *J.*, 1961, 2914.
[5] McCready and McComb, *Analyt. Chem.*, 1952, **24**, 1986.
[6] Killion and Foster, *J. Polymer Sci.*, 1960, **46**, 65.
[7] Vollmert, *Makromol. Chem.*, 1950, **5**, 110.
[8] Neukom and Deuel, *Z. schweiz. Forstv.*, 1960, **30**, 223.

acidic solution (cf. ref. 9). Vollmert [7] concluded that depolymerisation of pectic materials in alkali ceased when concurrent de-esterification became complete; recent work [10] has shown that only about one de-esterification in 80 leads to cleavage of a glycosidic linkage.

Less is known, however, of the possible modification suffered by pectic materials during extraction. Exhaustive extraction with hot 70% aqueous ethanol [11] and hot water usually precede the extraction of the pectic complex with hot oxalate solutions. This paper shows that some decarboxylation occurs during each of these stages.

In studies of the various methods of decarboxylating uronic acids,[12] refluxing with de-ionised water caused complete decarboxylation of galacturonic acid in about 80 hours in a vessel continuously swept with carbon dioxide-free nitrogen. Kinetic studies of the evolution of carbon dioxide from some uronic acids were then made; these gave the results in Table 1 (it is there assumed that 1 mole of carbon dioxide resulted from decarboxylation of 1 mole of uronic acid and that all the carbon dioxide evolved came from carboxyl groups; under the experimental conditions the amounts of carbon dioxide liberated in

TABLE 1.

Decarboxylation (%) of uronic acids in boiling conductivity-grade water.

| Time ($10^3$ sec.) | Glucurone | Galact-uronic acid | Trigalact-uronic acid | Ca L-sorburonate | Alginic acid |
|---|---|---|---|---|---|
| 10 | 5·6 | 7·8 | 12·8 | 35·0 | 3·7 |
| 20 | 11·1 | 15·1 | 24·2 | 50·9 | 7·3 |
| 30 | 16·6 | 21·9 | 33·6 | 60·2 | 11·0 |
| 40 | 21·8 | 28·3 | 41·4 | 66·4 | 14·6 |
| 60 | 31·5 | 39·8 | 54·2 | 73·3 | 21·7 |
| 80 | 40·4 | 50·0 | 64·1 | 78·3 | 28·5 |
| 100 | 48·7 | 59·2 | 72·2 | 87·4 | 35·1 |
| 150 | 66·3 | 78·2 | 87·2 | 90·2 | 50·7 |
| 200 | 79·4 | 91·4 | 96·0 | 96·4 | 65·6 |
| 250 | 88·4 | 97·8 | 99·4 | 98·3 | 79·4 |
| Hence $10^6 k_1$ (sec.$^{-1}$) = | 5·18 | 6·56 | 12·5 | 57·6 | 1·42 |

side reactions or from general degradation or decomposition would be expected to be very small; cf. ref. 1).

The rate constants ($k_1$) were calculated by Guggenheim's method.[13] (The results reported were obtained by using conductivity-grade water; traces of metal ions catalyse decarboxylation,[14] and results obtained by adding salts and other substances will be given elsewhere.)

Alginic acid was the most stable of the materials refluxed with water, yet 7% decarboxylation occurred in 5 hours (*i.e.*, the original uronic anhydride content was reduced from 97 to 90%). A total reflux period of 5 hours would not be excessive if exhaustive aqueous extraction were required; it is difficult to remove starch completely by aqueous extraction,[15] and the contamination of pectins by starch is well known.[16] The study of aqueous decarboxylation was therefore extended to a commercial apple pectin, pectic acids from *N. translucens* [17] and *C. australis*,[18] ammonium pectates from *N. translucens*,[17] and lucerne.[19] Reflux in aqueous solution for several hours caused significant decarboxylation, as shown by the percentages quoted in Table 2. The same Table shows also that some decarboxylation occurs on prolonged refluxing with 70% aqueous ethanol.

[9] Albersheim, Neukom, and Deuel, *Arch. Biochem. Biophys.*, 1960, **90**, 46.
[10] Launer and Tomimatsu, *J. Org. Chem.*, 1961, **26**, 541.
[11] Williams and Bevenue, *J. Assoc. Off. Agric. Chem.*, 1956, **39**, 901.
[12] Garbutt, Ph.D. Thesis, Univ. of Edinburgh, 1960.
[13] Guggenheim, *Phil. Mag.*, 1926, **2**, 538.
[14] Zweifel and Deuel, *Helv. Chim. Acta*, 1956, **39**, 662.
[15] Anderson and Greenwood, *J. Sci. Food Agric.*, 1955, **6**, 587.
[16] Bock, Baum, Döring, and Wardsack, *Ernährungsforsch.*, 1960, **5**, 539.
[17] Anderson and King, *Biochem. Biophys. Acta*, 1961, **52**, 441.
[18] Anderson and King, *Biochem. Biophys. Acta*, 1961, **52**, 449.
[19] Fanshawe, Ph.D. Thesis, Univ. of Edinburgh, 1960.

After exhaustive extraction with 70% ethanol and with hot water, pectic substances are usually extracted by repeated treatments at 80—90° with 0·5% aqueous ammonium oxalate.[11,19,20] The percentage decarboxylation caused by this reagent is shown in Table 2. In recent years, extraction with hot water containing 0·25% of oxalic acid and 0·25% of ammonium oxalate has been preferred for certain materials.[11,21] Our experiments have shown, however (see Table 2), that this extractant causes extensive decarboxylation. (Control determinations showed that the carbon dioxide evolved did not result from decomposition of the oxalate solution.)

The pectic acid and ammonium pectate samples studied had all been isolated by hot oxalate extraction of material which had been pretreated with 70% ethanol and with hot water, yet carbon dioxide was evolved from each sample on further treatment with

TABLE 2.

The apparent percentage of decarboxylation * of some pectic materials when treated with aqueous solutions used in extraction.

| Samples ‡ decarb-oxylated | Extractant and temperature | Period of extraction † (hours) 2 | 4 | 5 | 10 | 12 | 20 | 24 | 32 | 40 | 50 | 60 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | De-ionised water, b. p. | 2·7 | 4·1 | — | — | 5·0 | — | 6·1 | — | — | — | — |
| 2 | | 1·8 | 2·6 | — | — | 5·1 | — | 7·6 | — | — | — | — |
| 3 | | 0·9 | 1·6 | — | — | 4·2 | — | 9·4 | — | — | — | — |
| 4 | | 1·4 | 3·2 | — | — | 6·9 | — | 10·9 | — | — | — | — |
| 2 | 70% aq. ethanol, b. p. | — | 1·0 | — | — | — | 1·5 | — | — | — | 3·0 | — |
| 3 | | — | 1·5 | — | — | — | 2·3 | — | — | — | 4·1 | — |
| 5 | | — | 1·6 | — | 2·4 | — | 4·5 | — | 7·0 | — | 11·9 | — |
| 6 | | — | 1·8 | — | 3·4 | — | 6·2 | — | 9·1 | — | 14·6 | — |
| 7 | | — | 1·9 | — | 3·9 | — | 6·8 | — | 9·6 | — | 15·2 | — |
| 1 | 0·25% aq. ammonium oxalate + 0·25% aq. oxalic acid 85—90° | — | 4·9 | — | — | — | — | 28·0 | 34·2 | — | — | — |
| 2 | | 5·9 | 7·9 | — | — | — | — | 31·0 | 36·0 | — | — | — |
| 3 | | 2·7 | 3·8 | — | 5·9 | — | — | 14·4 | — | 24·0 | 28·0 | — |
| 4 | | 2·2 | 6·0 | — | — | — | — | 32·0 | 38·4 | — | — | — |
| 5 | | — | — | 4·6 | 7·5 | — | 14·3 | — | — | 26·6 | — | 36·2 |
| 6 | | — | — | 5·0 | 8·4 | — | 15·9 | — | — | 29·2 | — | 40·2 |
| 7 | | — | — | 5·8 | 10·1 | — | 19·4 | — | — | 36·1 | — | 48·8 |
| 1 | 0·5% aq. ammonium oxalate, 85—90° | 1·0 | — | — | 4·8 | 5·7 | — | 11·5 | — | — | — | — |
| 2 | | 5·0 | 6·6 | — | — | 10·0 | 12·0 | — | — | — | — | — |
| 3 | | 1·4 | — | — | — | 4·3 | — | 5·9 | — | — | — | — |
| 4 | | 1·6 | 2·6 | — | — | 6·1 | — | 9·6 | — | — | — | — |

* Values shown are the average of duplicate determinations made on each material under the stated conditions; agreement in the duplicate determinations was within ±10%.

† In presence of nitrogen.

‡ Origin of samples: 1, ammonium pectate from N. *translucens*;[17] 2, pectic acid from *C. australis*;[18] 3, commercial apple pectin; 4, ammonium pectate from lucerne;[19] 5, alginic acid;[23] 6, glucurone; 7, galacturonic acid.

these extractants. In view of the experimental conditions, it seems reasonable to postulate that this carbon dioxide arose from decarboxylation, although there may be a small contribution from general decomposition or degradation. Clearly, the samples must therefore have undergone decarboxylation to at least a similar extent during their original extraction from the plant material. The present results indicate that the customary extraction solutions cause decarboxylation of pectic materials to the following extent: (*a*) ~0·2% per hr. in refluxing 70% aqueous ethanol; (*b*) 0·4—0·6% per hr. in refluxing hot water; (*c*) 0·3—0·9% per hr. on extraction at 85—90° with 0·5% aqueous ammonium oxalate; (*d*) 1·4% per hr. on extraction with water containing 0·25% each of ammonium oxalate and oxalic acid at 85—90° for three laboratory-prepared specimens and 0·6—0·7% per hr. for commercial apple pectin. Contact with each hot extractant for 4 hours in the

[20] Aspinall and Cañas-Rodriguez, *J.*, 1958, 4020; Kertesz, "The Pectic Substances," Interscience Publ. Inc., New York, 1951, pp. 103—104; Adams and Castagne, *Canad. J. Chem.*, 1949, **27**, *B*, 924.

[21] Bishop, *Canad. J. Chem.*, 1955, **33**, 1521.

presence of nitrogen will cause a total of 3—6% decarboxylation if 0·5% aqueous ammonium oxalate is used; the total may reach 8% if the ammonium oxalate–oxalic acid treatment is employed. Increasing the extraction times increases the extent of the decarboxylation.

It is of interest that, in both the oxalate extractants, the commercial apple pectin (MeO = 5·1%) was more stable than the laboratory-prepared pectic acids, which contained no methoxyl. The closely related behaviour of the products from lucerne, *N. translucens*, and *C. australis* is interesting since the absence of methoxyl groups in the lucerne product was a consequence of de-esterification during isolation;[19] the products from *Nitella* and *Chara* came from algae whose cells contained no methoxyl.[17,18]

Previous workers[9,10] have established that the alkali-sensitivity of the 1,4-bonds in pectic materials depends on the presence of ester groups at position 6, the de-esterified product being practically stable to further degradation.[7,10] A second effect can now apparently be distinguished; de-esterified or initially non-esterified pectic materials are less stable to chemical modification than are esterified products.

Clearly, contact with any hot extractant must be as brief as possible if significant decarboxylation of pectic materials is to be avoided: in particular, hot oxalate–oxalic acid solutions cause considerable decarboxylation. If use of hot extraction solutions is unavoidable, the extent of the chemical modification suffered by the pectic material should be assessed, before structural studies, by decarboxylation experiments on the extracted material.

## Experimental and Results

*Origin of Samples.*—(*a*) D(+)-Galacturonic acid monohydrate (Roche Biochemicals Ltd.) (Found: C, 34·8; H, 5·7. $C_6H_{12}O_8$ requires C, 34·0; H, 5·7%) had 96% purity [decarboxylation[22] in 19% (w/w) hydrochloric acid for 2½ hr.]; paper chromatography showed a trace of galactose. (*b*) D-Glucurone (Roche Biochemicals Ltd.) (Found: C, 40·8, 40·7; H, 4·6, 4·6. $C_6H_8O_6$ requires C, 40·9; H, 4·6%) had 97·2% purity. (*c*) Alginic acid was the sample prepared by cold extraction by Chanda *et al.*,[23] which had 97·4% purity. (*d*) Trigalacturonic acid and calcium 5-oxo-D-gluconate (calcium L-sorburonate) were kindly provided by Dr. W. W. Reid.[24] The former was free from mono- and di-galacturonic acid but contained a small quantity of a polygalacturonic acid (detected by chromatography); it had 95·0% purity. The 5-oxo-D-gluconate was 93% pure. (*e*) Commercial apple pectin (B.D.H. Ltd., 240 grade) had uronic anhydride[22] 58%, OMe[25] 5·1%. (*f*) Ammonium pectate from *Nitella translucens*[17] had no methoxyl content,[25] uronic anhydride[22] 51%. (*g*) Ammonium pectate from lucerne[19] had no methoxyl and 51% of uronic anhydride. (*i*) Pectic acid from *Chara australis*[18] had no methoxyl and 52% of uronic anhydride.

*Apparatus.*—Anderson's decarboxylation apparatus and reaction conditions[22] were used. A reaction flask, having a thermometer-pocket sealed into the flask-wall, was used in experiments where temperatures other than reflux temperature were used. Kinetic measurements were facilitated by fitting a two-way stop-cock after $T_2$ (see ref. 22) so that the gas stream could be switched from one absorption trap to a second identical trap. A matched pair of traps was used; in these, the sintered discs had closely matching porosity so that identical back pressures, and hence constant reflux temperatures, were maintained. The nitrogen flow-rate was stabilised by a capillary-buffer system, needle valves, and a Rotameter.

*Decarboxylation of Uronic Acids in Water.*—Conductivity-grade water from a laboratory de-ioniser was refluxed in the decarboxylation apparatus, then allowed to cool in an atmosphere of carbon dioxide-free nitrogen. The weighed sample of uronic acid was added to the reaction flask. The carbon dioxide evolved was determined at intervals during the refluxing; the results are shown in Table 1. Control experiments confirmed that carbon dioxide was not evolved when water alone was refluxed. The decarboxylation of uronic acids in acid solution has been shown to be of the first order;[12] on the assumption that this applies also to aqueous

[22] Anderson, *Talanta*, 1959, **2**, 73.
[23] Chanda, Hirst, Percival, and Ross, *J.*, 1952, 1833.
[24] Brooks and Reid, *Chem. and Ind.*, 1955, 325, 360; Jones and Reid, *Canad. J. Chem.*, 1955, **33**, 1682.
[25] Anderson and Duncan, *Talanta*, 1961, **8**, 241.

solutions, the rate constants shown in Table 1 were calculated by Guggenheim's method,[13] which does not require a knowledge of the precise purity of the substrates.

*Decarboxylation of Pectic Materials in Hot Water.*—Samples (110—190 mg.) of commercial apple pectin, ammonium pectates from *N. translucens* and lucerne, and pectic acid from *C. australis* were refluxed with conductivity-grade water; the carbon dioxide evolved was determined at intervals up to 24 hr. from the start of refluxing. It has been shown [1] that 98% of the carbon dioxide liberated when uronic acid materials are refluxed in acid solution comes from the carboxyl groups. On the assumption that this will also hold for aqueous solutions, yields of carbon dioxide were expressed as percentage decarboxylation. The results from the hot-water experiments are shown in Table 2. Each result is the average of duplicate runs made with the substance named; agreement to within $\pm 10\%$ was always obtained.

*Decarboxylation in Aqueous 70% Ethanol.*—Samples (120—200 mg.) of galacturonic acid, glucurone, alginic acid, commercial apple pectin, and pectic acid from *C. australis* were refluxed with 70% aqueous ethanol, and the carbon dioxide liberated was determined at intervals up to 50 hr. from the start of refluxing. A very small amount of carbon dioxide was evolved when 70% aqueous ethanol was refluxed alone ($\geqslant 5\%$ of that evolved when substrates were present) and the yields of carbon dioxide obtained were corrected for this. On the assumption that the corrected yield of carbon dioxide came from carboxyl groups, the results are shown in Table 2.

*Decarboxylation in 0·25% Aqueous Ammonium Oxalate + 0·25% Oxalic Acid Solution at 85—90°.*—Samples (100—150 mg.) of galacturonic acid, glucurone, alginic acid, commercial pectin, pectic acid from *C. australis*, and ammonium pectates from lucerne and *N. translucens* were treated with water containing 0·25% each of ammonium oxalate and oxalic acid, maintained at 85—90°. The carbon dioxide liberated was determined at intervals up to 60 hr. The yields of carbon dioxide were corrected for the very small amounts of carbon dioxide detected when the hot oxalate solution alone was maintained at 90°. The percentages shown in Table 2 were obtained from calculations based on the corrected yields of carbon dioxide.

*Decarboxylation with Aqueous 0·5% Ammonium Oxalate at 85—90°.*—Samples (100—150 mg.) of commercial apple pectin, ammonium pectate from lucerne and *N. translucens*, and pectic acid from *C. australis* were treated at 85—90° with 0·5% aqueous ammonium oxalate. The carbon dioxide evolved was determined at intervals up to 24 hr. from the start of refluxing. Very small amounts of carbon dioxide were detected when the ammonium oxalate solution alone was kept at 90°. The percentages shown in Table 2 were calculated from the corrected yields of carbon dioxide.

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## 1034. *The Composition of* Afraegle paniculata *Mucilage.*

By F. G. TORTO.

*Afraegle paniculata* mucilage gives on hydrolysis D-galactose, L-arabinose, L-rhamnose, and D-glucuronic acid. Partial hydrolysis of the mucilage gives an aldobiouronic acid, 6-O-β-D-glucuronosyl-D-galactose.

*Afraegle paniculata* Engl. (family Rutaceae) is an evergreen tree occurring in savannah country near the sea in Ghana. It bears fruits resembling grapefruit in size and appearance. The insides of the fruits are divided into segments like those of an orange, each segment holding several seeds immersed in a sticky mucilage.

Purified *Afraegle paniculata* mucilage has a small positive specific rotation and an equivalent weight of 4000, indicating the presence of a small proportion of acidic residues. On complete hydrolysis, D-galactose, L-arabinose, L-rhamnose, and D-glucuronic acid are obtained.

XUM

Paper chromatography of the products of hydrolysis by 0·02N-sulphuric acid at 95° showed the liberation within 2 hours of arabinose, and after 6 hours of galactose and rhamnose, indicating that arabinose is present in the furanose form or is located at peripheral positions in the polysaccharide molecule.

Partial hydrolysis of the mucilage gave a product containing an aldobiouronic acid which was shown to be homogeneous by prolonged chromatography in an acid solvent and migrated at the same rate on the chromatogram as 6-*O*-β-D-glucuronosyl-D-galactose isolated from gum arabic.

The aldobiouronic acid was shown to be 6-*O*-β-D-glucuronosyl-D-galactose by oxidation of the galactose moiety with bromine, and by isolation of 2,3,4-tri-*O*-methyl-D-galactose from the hydrolysis products of the fully methylated form.

The optical rotation of the aldobiouronic acid indicates that a β-glucuronosyl junction. The mucilage thus bears a superficial resemblance to *Acacia* gums.[1,2]

## Experimental

Paper chromatograms were run in the solvent systems (A) butan-1-ol–ethanol–water (5 : 1 : 4 v/v, upper phase), (B) butan-1-ol–ethanol–water (20 : 1 : 3) with added cetylpyridinium bromide (3 g./100 c.c.), (C) ethyl acetate–acetic acid–formic acid–water (18 : 3 : 1 : 4), (D) butanol–benzene–pyridine–water (5 : 1 : 3 : 3), and (E) ethyl methyl ketone saturated with water. Spots were detected with an aqueous aniline oxalate spray.

Optical rotations were determined for water solutions.

*Purification of the Mucilage.*—The fruits were opened and the segments containing the seeds and mucilage were separated from the brown pulp. The segments were split and the mucilage pressed out, care being taken to avoid contamination with other parts of the fruit.

The mucilage from 30 fruits was made up with distilled water to about 1 l. and added to methanol (3·5 l.). The precipitated material, collected on filter paper, dried to a thick gel (180 g.) in air.

A portion (20 g.) of the crude gel was purified by precipitation: solutions, twice in dilute hydrochloric acid and then once in water, were poured with stirring into methanol. The product, after drying at 30° in a partial vacuum ($CaCl_2$) for 48 hr., was a white amorphous powder (11 g.), $[\alpha]_D^{23}$ +2·5° (*c* 0·3) [Found: equiv., 4000 (by titration); ash, 0].

*Total Hydrolysis.*—The purified mucilage was completely hydrolysed by heating a 0·5% solution in 2N-sulphuric acid in a sealed tube in a boiling-water bath for 24 hr. The solution was neutralised with barium carbonate, filtered, and concentrated under reduced pressure to small volume. On chromatograms with reference substances run in several solvent systems, the sugars galactose, arabinose, and rhamnose were detected. The mucilage was extensively decomposed during the hydrolysis, but an approximate estimate of the proportions of sugars present was obtained by comparing the areas of spots on a chromatogram with those formed by solutions of sugars of known concentration. This gave the galactose : arabinone : rhamnose ratio of 4 : 3 : 2 (very approximate values owing to the prior decomposition).

*Isolation of the Aldobiouronic Acid.*—Purified mucilage (75 g.) was heated in N-sulphuric acid (600 c.c.) at 100° for 24 hr. The filtered solution was neutralised with barium carbonate and again filtered and the filtrate was concentrated under reduced pressure to a syrup (100 c.c.). This was poured into methanol (1 l.), and the precipitated barium salt purified by reprecipitation in methanol from aqueous solution, giving a cream solid (4·5 g.), $[\alpha]_D^{23}$ +2° ± 5° (*c* 2·5) (Found: Ba, 16·9. Calc. for $C_{12}H_{17}Ba_{0·5}O_{12}$: Ba, 16·2%). Prolonged chromatography (104 hr.) of the barium aldobiouronate in solvent D gave only one spot, indicating homogeneity. The rate of migration in solvent C ($R_{gal.}$ *ca.* 0·25) was the same as that of 6-*O*-β-D-glucurosonyl-D-galactose, from gum arabic, run on the same paper.

Upon hydrolysis of the barium salt with 2N-sulphuric acid in a sealed tube at 100° for 16 hr., the neutralised and de-ionised [I.R.-120($H^+$)] solution was examined on a chromatogram. Galactose, glucuronic acid, and glucurone were identified.

*Isolation of Galactose, Arabinose, and Rhamnose.*—Concentration of the methanolic mother liquors from the precipitation of the barium aldobiouronate, and storage at 0°, yielded crude crystalline galactose. Purified by recrystallisation from methanol, it had m. p. and mixed

[1] Hirst and Perlin, *J.*, 1954, 2622.
[2] Charlson, Nunn, and Stephen, *J.*, 1955, 169.

m. p. 162—165°, $[\alpha]_D^{23}$ +80° (*c* 0·5), and gave mucic acid, m. p. and mixed m. p. 212—214°, on oxidation with nitric acid.

A portion of the syrup left after the removal of galactose was separated on a large paper chromatogram, and L-arabinose, m. p. and mixed m. p. 156°, $[\alpha]_D^{23}$ +104° (*c* 0·5) [benzoylhydrazone, m. p. and mixed m. p. 206—207° (from ethanol)], and α-L-rhamnose hydrate (from ethanol), m. p. and mixed m. p. 93—94°, $[\alpha]_D^{23}$ +10° (*c* 1·5), were obtained.

*Identification of Uronic Acid.*—Barium aldobiouronate (0·400 g.) was heated with 2N-sulphuric acid (5 c.c.) in a sealed tube at 100° for 24 hr. The neutralised solution was evaporated to a light syrup and poured into methanol. The precipitated barium uronate was removed on the centrifuge and purified by two reprecipitations in methanol from aqueous solution. The product was a cream powder (0·083 g.), $[\alpha]_D^{21}$ +15° (*c* 0·3) (Found: Ba, 26·7. Barium hexouronate requires Ba, 26·2%).

When de-ionised with I.R.-120($H^+$) resin, it gave glucuronic acid and glucurone on chromatograms run in several solvents with authentic reference substances. Complete lactonisation was effected by heating it in a vacuum at 70° for several hours; the product was converted into the *p*-nitroanilide,[3] m. p. and mixed m. p. 129—130°, of glucuronic acid.

*Structure of the Aldobiouronic Acid.*—A specimen of barium aldobiouronate was oxidised with bromine water for a week and the bromine was removed by aeration. The product was hydrolysed with 1·75N-sulphuric acid at 100° for 24 hr., neutralised, and de-ionised with I.R.-120($H^+$) resin. On a paper chromatogram run in solvent (B) only uronic acid was detected.

Barium aldobiouronate (1·7 g.) was methylated four times with dimethyl sulphate and alkali. The product, after acidification of the reaction mixture, was isolated by continuous extraction with chloroform and then methylated twice with methyl iodide and silver oxide. The product, a viscous syrup (1·0 g.), was distilled, giving a main fraction (0·5 g.), b. p. 180°/0·01 mm., $n_D^{26}$ 1·4655 (Found: C, 50·8; H, 7·7; OMe, 50·1. Calc. for $C_{20}H_{36}O_{12}$: C, 51·3; H, 7·8; 8OMe, 53·0%). The syrup (0·450 g.) was heated with 2N-sulphuric acid in a sealed tube at 100° for 24 hr. The filtered solution was neutralised with sodium hydroxide solution and extracted in a continuous extractor with ethyl acetate. The extract, on evaporation, gave a syrup (0·090 g.), which on the chromatogram gave a spot corresponding to 2,3,4-tri-*O*-methylgalactose as well as a trace of tetra-*O*-methylgalactose. The syrup was separated on a large paper chromatogram, 2,3,4-tri-*O*-methylgalactose, $[\alpha]_D^{23}$ +95° (*c* 0·5), being obtained. Its identity was confirmed by preparation of the crystalline *N*-phenyl-D-galactosylamine trimethyl ether, m. p. and mixed m. p. 162—163°, and by oxidation with sodium periodate, giving formaldehyde (dimedone compound, m. p., and mixed m. p., 192°).

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UNIVERSITY COLLEGE OF GHANA, LEGON, GHANA. [*Received, May 15th,* 1961.]

[3] Hamilton, Spriestersbach, and Smith, *J. Amer. Chem. Soc.*, 1957, **79**, 443.

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## 1035. *Organic Peroxides. Part VI.*[1] *The Decomposition of* p-*Nitrophenyldiphenylmethyl Peroxides.*

By J. I. G. CADOGAN, D. H. HEY, and W. A. SANDERSON.

Thermal decomposition of t-butyl *p*-nitrophenyldiphenylmethyl peroxide in *p*-xylene and of bis-(*p*-nitrophenyldiphenylmethyl) peroxide in bromobenzene gives benzophenone, *p*-nitrophenol, *p*-nitrobenzophenone, and phenol. No evidence for the formation of free *p*-nitrophenyldiphenylmethoxy-radicals was obtained.

KHARASCH, Poshkus, Fono, and Nudenberg,[2] in a study of the thermal decomposition of t-butyl triarylmethyl peroxides (I) in cumene, concluded that triarylmethoxy-radicals

[1] Part V, Cadogan, Hey, and Sanderson, *J.*, 1961, 3879.
[2] Kharasch, Poshkus, Fono, and Nudenberg, *J. Org. Chem.*, 1951, **16**, 1458.

(II) were first formed and then rearranged, as described by Wieland,[3] to give aryloxydiphenylmethyl radicals (III; Ar = *p*-$CH_3 \cdot C_6H_4$, α-$C_{10}H_7$, *p*-$Ph \cdot C_6H_4$), which eventually formed the dimer (IV). Subsequent reaction of the latter with α-cumyl radicals is then claimed to give the ether (V).

*p*-Nitrophenyldiphenylmethyl t-butyl peroxide (I; Ar = *p*-$NO_2 \cdot C_6H_4$) behaved differently and only benzophenone and *p*-nitrophenol were isolated. This anomalous

$ArCPh_2 \cdot O \cdot O \cdot CMe_3$ (I) $\quad ArCPh_2 \cdot O\cdot$ (II) $\quad Ph_2\dot{C} \cdot OAr$ (III)

$Ph_2C(OAr) \cdot Ph_2C(OAr)$ (IV) $\quad Ph_2C(OAr) \cdot Ph \cdot CMe_3$ (V) $\quad Ar \cdot CPh_2 \cdot O \cdot O \cdot CPh_2 \cdot Ar$ (VI)

reaction has been reinvestigated because a possible mode of decomposition, apparently ignored by Kharasch and his co-workers,[2] could involve the *p*-nitrophenyldiphenylmethoxy-radical, which in turn could give benzophenone and a *p*-nitrophenyl radical, and/or *p*-nitrobenzophenone and a phenyl radical.

In theory *p*-nitrophenyldiphenylmethyl t-butyl peroxide (I; Ar = *p*-$NO_2 \cdot C_6H_4$) on decomposition can produce two different alkoxy-radicals. In an attempt to overcome this complication the hitherto unknown bis-(*p*-nitrophenyldiphenylmethyl) peroxide

(VI) → $Ph_2CO + ArO \cdot CPh_2Ar$ (VII)
(VI) → $ArCOPh + PhO \cdot CPh_2Ar$ (VIII)

(VI; Ar = *p*-$NO_2 \cdot C_6H_4$), which on decomposition might be expected to produce two *p*-nitrophenyldiphenylmethoxy-radicals, has been prepared and allowed to decompose in bromobenzene at 115°. No free-radical arylation of the solvent was detected but *p*-nitrophenol (0·32 mole/mole of peroxide), benzophenone (0·35), phenol (0·04), and *p*-nitrobenzophenone (0·02), were isolated. The correspondence between the yields of phenol and ketone implies that their formation by rearrangement of a single *p*-nitrophenyldiphenylmethoxy-radical, if indeed it is formed, does not occur, since there is insufficient oxygen in the radical. It appears more likely that these products may be formed by way of the ethers (VII) and (VIII), although no direct evidence on the point is available. The hydrogen needed for phenol and *p*-nitrophenol formation does not arise from the solvent, for this would have given rise to dibromobiphenyls. No product derived from a Wieland rearrangement was detected.

In view of these results the decomposition of t-butyl *p*-nitrophenyldiphenylmethyl peroxide (I; Ar = *p*-$NO_2 \cdot C_6H_4$), was reinvestigated. *p*-Xylene, rather than cumene, was used as the solvent because the formation of aryl radicals is more easily detected in this case, there being only one product of substitution. Again, no arylation occurred and *p*-nitrophenol (0·59 moles/mole peroxide), benzophenone (0·44), phenol (0·13), and *p*-nitrobenzophenone (0·12) were formed. Kharasch *et al.*[2] did not report the formation of phenol and *p*-nitrobenzophenone. On the other hand, Bartlett and Cotman[4] reported that thermal decomposition of the related *p*-nitrophenyldiphenylmethyl hydroperoxide gave *p*-nitrophenol, phenol, and *p*-nitrophenyldiphenylmethanol but no benzophenone, and concluded that radicals were intermediates in the reaction. We have no evidence in favour of a homolytic mechanism for the decomposition of the peroxides described in this paper.

## Experimental

*Preparation of Compounds.*—*p*-Nitrobenzophenone, m. p. 137—139°, prepared by Schroeter's method,[5] was converted into *p*-nitrophenylphenyldichloromethane, yellow crystals, m. p.

[3] Wieland, *Ber.*, 1911, **44**, 2550.
[4] Bartlett and Cotman, *J. Amer. Chem. Soc.*, 1950, **72**, 3095.
[5] Schroeter, *Ber.*, 1909, **42**, 3356.

55—57°, from light petroleum (b. p. 40—60°), as described by Baeyer and Villiger,[6] who reported m. p. 56—57°. Treatment of the dichloride with benzene and aluminium chloride and subsequent recrystallisation of the product from light petroleum (b. p. 100—120°) gave *p*-nitrophenyldiphenylmethyl chloride, m. p. 90—93°. Baeyer and Villiger [6] reported m. p. 92—93°. The following method of conversion of the above chloride into the corresponding carbinol was found to be more convenient than those of Baeyer and Villiger [6] and of Bartlett and Cotman.[4] The crude chloride (80 g.) in ethanol (200 ml.) was boiled under reflux with potassium hydroxide (16·5 g.) in ethanol (100 ml.) for 30 min. Water (200 ml.) was added to the cooled solution to precipitate *ethyl* p-*nitrophenyldiphenylmethyl ether*, which crystallised from aqueous methanol as pale yellow crystals (45 g.), m. p. 105—107° (Found: C, 75·8; H, 5·5. $C_{21}H_{19}NO_3$ requires C, 75·7; H, 5·7%). The ether (20 g.) in acetic acid (200 ml.) was treated with perchloric acid (70%; 70 ml.). Water (100 ml.) was added to precipitate *p*-nitrophenyldiphenylmethanol, which on recrystallisation from light petroleum (b. p. 100—120°) had m. p. 98·5—100°. Bartlett and Cotman [4] reported m. p. 97—98°. Bis-(*p*-nitrophenyldiphenylmethyl) peroxide was prepared by stirring the carbinol (8 g.) in ether (30 ml.) with sulphuric acid (*d* 1·8; 0·15 ml.) and hydrogen peroxide (86% w/w; 15 ml.) for 24 hr. Special precautions against explosion were taken.* Water (50 ml.) was added and the mixture was separated and washed with ether. The ether solution was washed with alkali and dried ($Na_2SO_4$). Evaporation of the solution left crude *p*-nitrophenyldiphenylmethyl hydroperoxide (8·6 g.; 90% hydroperoxide content [7]) as a yellow viscous liquid, which slowly (7 days) solidified. The crude hydroperoxide (4 g.) and *p*-nitrophenyldiphenylmethanol (4 g.) in acetic acid (20 ml.) were treated with sulphuric acid (*d* 1·8; 0·2 ml.) in acetic acid (10 ml.) at 80° for 1 hr. Filtration of the hot mixture and recrystallisation of the residue from chloroform–ethanol gave *bis*-(p-*nitrophenyldiphenylmethyl*) *peroxide* (1·7 g.), m. p. 182° (decomp.) (Found: C, 74·4; H, 4·7; N, 4·6. $C_{38}H_{28}N_2O_6$ requires C, 75·0; H, 4·6; N, 4·6%). The acetic acid filtrate deposited *p*-nitrobenzophenone (1·7 g.), m. p. and mixed m. p. 136—137°.

*p*-Nitrophenyldiphenylmethyl t-butyl peroxide crystallised as yellow needles, m. p. 123—124°, from chloroform–ethanol. Kharasch *et al.*[2] reported m. p. 119°.

*Decomposition of Bis-*(p-*nitrophenyldiphenylmethyl*) *Peroxide in Bromobenzene.*—The peroxide (2·504 g.) in bromobenzene (150 ml.) was kept under nitrogen at 115° for 3 days. After removal of the solvent the residue was distilled (0·1 mm.) to give the following fractions: (*a*) a colourless oil (0·015 g.; b. p. <100°), (*b*) a pale yellow oil (0·456 g.; b. p. 100—120°), and left a residue (*c*) (1·972 g.; b. p. >180°). The infrared spectrum of fraction (*a*) indicated the presence of benzophenone and phenol only. A portion (0·331 g.) of fraction (*b*) on chromatography on alumina gave benzophenone (0·189 g.), m. p. and mixed m. p. 45—47° and *p*-nitrobenzophenone (0·008 g.), identified by its infrared spectrum. Elution with methanol gave sodium *p*-nitrophenoxide (0·036 g.), identified by its infrared spectrum, formed by interaction of *p*-nitrophenol with alkali present in the alumina. Chromatography of the residue from the distillation, and examination of the spectra of the eluted fractions, indicated the presence of many unidentified products. Only one fraction (elution with benzene) appeared to be homogeneous and gave a yellow solid (0·099 g.), which after recrystallisation from ethanol had m. p. 205—210° (Found: C, 68·2; H, 4·4%). The infrared spectrum indicated the presence of the arylalkyl ether linkage (8·05—8·3μ; 9·9μ) and the nitro-group.

*Decomposition of* p-*Nitrophenyldiphenylmethyl t-Butyl Peroxide in* p-*Xylene.*—The peroxide (4·000 g.) in *p*-xylene was kept under nitrogen at 115° for 3 days. Extraction with 4N-sodium hydroxide gave impure *p*-nitrophenol (0·403 g.), which on recrystallisation from toluene had m. p. and mixed m. p. 112—114°. The infrared spectrum of the impure product showed no evidence of the presence of phenol. After removal of *p*-xylene the residue was distilled at 0·1 mm. to give the following fractions: (*a*) a yellow liquid (0·134 g.; b. p. 42°), (*b*) a mixture of a colourless solid and orange oil (2·754 g.; b. p. 90—212°), and a black residue (0·782 g.; b. p. >250°). Fraction (*a*) was shown to be phenol (benzoate, m. p. and mixed m. p. 69—71°). Fraction (*b*) (1·130 g.) on chromatography on alumina gave only sodium *p*-nitrophenoxide (0·22 g.) and *p*-nitrobenzophenone (0·12 g.), m. p. and mixed m. p. 136—139°, and impure

* It should be noted that mixtures containing organic material and hydrogen peroxide of this strength sometimes result in explosion (see Criegee and Dietrich, *Annalen*, 1948, **560**, 135), although some twenty experiments of the type described above were carried out without incident.

[6] Baeyer and Villiger, *Ber.*, 1904, **37**, 597.
[7] Davies, Foster, and White, *J.*, 1953, 1541.

benzophenone (0·401 g.) as identified products. The presence of benzophenone was confirmed by its conversion into the 2,4-dinitrophenylhydrazone, m. p. and mixed m. p. 236—238°, and by its infrared spectrum. The impurities present in the benzophenone fraction were isolated by fractional crystallisation. With ethanol a trace of a nitro-compound, m. p. 161·5—162·5° (Found: C, 77·5; H, 5·6; N, 4·7%), was obtained, while light petroleum (b. p. 40—60°) gave a colourless crystalline compound, m. p. 50—51°, which depressed the m. p. of benzophenone (Found: C, 87·0; H, 6·5%).

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## 1036. *The Oxidation of Ethers and Related Compounds. Part I. The Thermal and Photochemical Decomposition of t-Butyl Peroxide in Anisole.*

By H. B. HENBEST, J. A. W. REID, and C. J. M. STIRLING.

Thermal decomposition of t-butyl peroxide in an excess of anisole at 140° has been shown to give mixtures of isomeric methoxytoluenes and phenoxymethylanisoles, but no 1,2-diphenoxyethane. These results, together with the high proportion of *ortho*-isomer in the phenoxymethylanisole mixture, are consistent with the initial production of phenoxymethyl radicals, which are sufficiently reactive at 140° to attack anisole at nuclear positions. As a further example of the reaction, 2,5-dimethoxybenzyl *p*-methoxyphenyl ether was obtained from the thermal decomposition of t-butyl peroxide in 1,4-dimethoxybenzene.

By contrast, the photochemical decomposition of t-butyl peroxide in anisole at 40° yielded no methoxytoluenes but gave 1,2-diphenoxyethane together with the isomeric phenoxymethylanisoles. The increasing order of reactivity of methyl groups towards t-butoxy-radicals at 140° is CMe, OMe, NMe; reasons for the differences are discussed.

CERTAIN atoms containing an unbonded electron pair are known to promote the attack of radical reagents at adjacent C–H bonds. Thus, tertiary alkylamines with t-butoxy-radicals give dialkylamino-substituted radicals that dimerise to derivatives of ethylenediamine [1] or, in the presence of oct-1-ene, add to this olefin.[2] In a study of benzyl ethers, Huang [3] has shown that t-butoxy-radicals cause a similar abstraction–dimerisation, but this cannot be strictly compared with the amine reactions because similar dimerisation *via* benzyl carbon occurs with toluenes in reaction with t-butyl peroxide,[4] *i.e.*, in the absence of the ether group.

Previous work with simpler ethers has been chiefly concerned with their reactions with acyl peroxides, especially benzoyl peroxide. Cass [5] showed that benzoyl peroxide reacts rather readily with dialkyl ethers, the products, formed in good yields, being benzoic acid and the α-benzoyloxy-ether. Kinetic studies [6,7] show that the peroxide decomposes both

[1] Henbest and Patton, *J.*, 1960, 3557.
[2] Urry and Juveland, *J. Amer. Chem. Soc.*, 1958, **80**, 3322.
[3] Huang and Si-Hoe, "Vistas in Free Radical Chemistry," Pergamon Press, London, 1959, p. 242.
[4] Wilen and Eliel, *J. Amer. Chem. Soc.*, 1958, **80**, 3309, and references therein.
[5] Cass, *J. Amer. Chem. Soc.*, 1947, **69**, 500.
[6] Cass, *J. Amer. Chem. Soc.*, 1946, **68**, 1976.
[7] Nozaki and Bartlett, *J. Amer. Chem. Soc.*, 1946, **68**, 1686.

unimolecularly and by an induced chain mechanism, and tracer studies [8] have established that the first-formed ether radical attacks predominantly the peroxide oxygen of the peroxide in the induced decomposition.

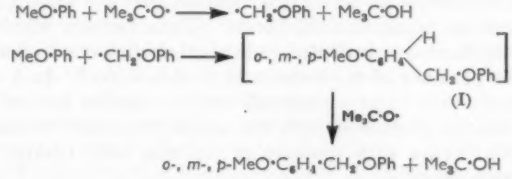
The reactions of alkoxy-radicals should in some ways be simpler than those of acyloxy-radicals, and the decomposition of t-butyl peroxide in anisole was chosen for investigation, this ether being the oxygen analogue of the previously studied dimethylaniline. Kinetic measurements have shown [7] that the decomposition of benzoyl peroxide in anisole is not a chain reaction, suggesting that nuclear substitution occurs in preference to abstraction of hydrogen from the methyl group, and this is supported by the isolation of methoxybiphenyls.[9] The methyl affinity [10] of anisole, however, is *less* than that of benzene. An interpretation of this result is that both hydrogen abstraction from the methyl group and nuclear substitution occur with methyl radicals.

The decomposition of t-butyl peroxide in anisole has been previously investigated by Cowley, Norman, and Waters,[11] who isolated (by vapour-phase chromatography, in unstated yield) an isomeric mixture of methoxytoluenes. The percentage composition of this mixture was shown to be: *o*- 74, *m*- 15, and *p*- 11. More recently, Johnston and Williams,[12] who made no reference to this previous work, obtained only " a dark involatile residue " on reaction of t-butyl peroxide with anisole.

We have investigated the decomposition of t-butyl peroxide in anisole induced thermally at 140° and photochemically at 40°, with ether and peroxide in the molar ratio of 10 : 1.

The thermal reaction, which was allowed to go to completion, gave isomeric mixtures of methoxytoluenes (*ca.* 29% based on acetone formed) and phenoxymethylanisoles (12% yield, see below). t-Butyl alcohol and acetone in the molar ratio 1·64 : 1 were also isolated, in 90% yield, together with small amounts of *o*-methoxybenzaldehyde and phenol. Careful examination failed to reveal any 1,2-diphenoxyethane and the remainder of the product consisted of resin from which no pure compound was isolated.

The identity of the phenoxymethylanisole fraction was demonstrated by hydrogenolysis and reduction by lithium–ammonia, which gave phenol and a mixture of isomeric methoxytoluenes in which the presence of the *ortho*- and *para*-isomers was shown by vapour-phase chromatography. The proportion (%) of each phenoxymethylanisole isomer (determined by vapour-phase chromatography which gave more satisfactory results in this instance than infrared analysis) was *o*- 70, *m*- 21, and *p*- 9. Phenoxymethylanisoles are considered to arise from nuclear substitution in anisole by phenoxymethyl radicals, which result from hydrogen abstraction from the methyl group of anisole by butoxy- or, to a smaller extent, by methyl radicals.

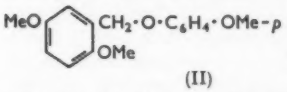



The 12% yield of phenoxymethylanisoles is based on peroxide and these schemes; if the intermediate (I) is dehydrogenated by a process, *e.g.*, disproportionation, other than abstraction of hydrogen by a butoxy- or a methyl radical, the percentage yield given is too high. This scheme is supported by the isomer distribution which is typical of homolytic aromatic substitution [13] and may be compared with the values for methylation [11] and

[8] Denney and Feig, *J. Amer. Chem. Soc.*, 1959, **81**, 5322; Drew and Martin, *Chem. and Ind.*, 1959, 925.
[9] Suehiro, *J. Chem. Soc. Japan*, 1951, **72**, 301.
[10] Heilman, Rembaum, and Szwarc, *J.*, 1957, 1127.
[11] Cowley, Norman, and Waters, *J.*, 1959, 1799.
[12] Johnston and Williams, *J.*, 1960, 1168.
[13] Augood and Williams, *Chem. Rev.*, 1957, **57**, 123.

phenylation [9] of anisole. Phenylation yields isomeric methoxybiphenyls in the ratio $o : m : p = 67 : 18 : 15$. Although the isomer ratios for phenoxymethylation, methylation, and phenylation of anisole are in good agreement, the values for phenoxymethylation do not necessarily indicate quantitatively the relative reactivities of the nuclear positions of anisole towards phenoxymethyl radicals, as the extent of further reactions of the phenoxymethylanisoles may vary with each isomer.

Material of higher molecular weight constituted the bulk of the product from the anisole–peroxide reaction at 140°. Much of this may arise from subsequent attack of radicals on the phenoxymethylanisoles, as reactions carried out with a 50 : 1 molar ratio of anisole to peroxide gave nearly twice the yield of the primary product. Subsequent attack can be envisaged to occur (i) by further nuclear substitution which would be slightly favoured with respect to anisole, and (ii) by abstraction of the benzyl hydrogen atom and dimerisation of the resulting radical. The latter reaction is known to occur with aryl benzyl ethers.[3] The radicals formed by hydrogen removal from the phenoxymethylanisoles may also decompose into other radicals, and the small amounts of phenol and *o*-methoxybenzaldehyde that were isolated probably arose in this way. Benzyl phenyl ether is known [14] to decompose, when heated, with formation of phenol and benzaldehyde, the reaction probably involving removal of benzyl hydrogen. The outcome of the anisole–peroxide reaction suggested that compound (II) should be the only primary product from the oxidation of 1,4-dimethoxybenzene. It was obtained in 19% yield (based on peroxide), its structure being confirmed by an alternative synthesis. Again, the major part of the product consisted of higher-boiling material.



(II)

The photochemically induced decomposition of t-butyl peroxide in anisole was carried out at 40° by irradiation with a mercury-arc lamp (principal wavelength 2570 Å). The products were markedly different from those obtained in the thermal reaction: 1,2-diphenoxyethane (11%) was obtained in addition to phenoxymethylanisoles (2%; essentially the *ortho*-isomer) (both yields based on peroxide consumed), and neither acetone nor methoxytoluene was detected. The yield of product of higher molecular weight was considerably lower than in the thermal reaction.

These results indicate that, at 140°, removal of phenoxymethyl radicals by nuclear substitution in anisole is too rapid to allow the occurrence of dimerisation, the rate of which depends on the square of the radical concentration. At 40°, however, nuclear substitution, with a higher energy of activation, becomes slower relative to dimerisation which consequently becomes observable. Moreover, it is concluded that alkyl radicals with an adjacent oxygen atom are considerably more reactive and hence shorter-lived than their nitrogen analogues which survive in a dialkylaniline solvent at 140° long enough to dimerise.[1]

This conclusion is supported by the observations that in *p*-methylanisole, butoxy-radicals abstract hydrogen from the *C*-methyl group [12] while in *NN*-dimethyl-*p*-toluidine, hydrogen is lost from an *N*-methyl group.[1] Further, when t-butyl peroxide was allowed to decompose in an equimolecular mixture of anisole and dimethylaniline, no *net* reaction with anisole was detected.

The reactivity of methyl groups towards t-butoxy-radicals increases in order CMe, OMe, NMe, as adduced by the yields of t-butyl alcohol (from reactions at 140°): 26% from t-butylbenzene,[15] *ca.* 55% from anisole, 100% from dimethylaniline,[1] and by the above competitive experiment. The greater reactivity of amines than of ethers is probably due to the greater capacity of amines to contribute a polar structure to the transition state (cf. the resonance polar effect discussed by Mayo and Walling [16] and Russell [17]). Electron

[14] Elkobaisi and Hickinbottom, *J.*, 1959, 1873.
[15] Raley, Rust, and Vaughan, *J. Amer. Chem. Soc.*, 1948, **70**, 1336.
[16] Mayo and Walling, *Chem. Rev.*, 1950, **46**, 191.
[17] Russell, *Tetrahedron*, 1959, **5**, 101; 1960, **8**, 101.

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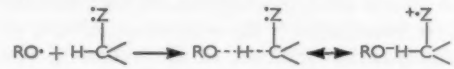
donation from the hetero-atom, with consequent lowering of the activation energy, occurs more readily when Z is nitrogen instead of oxygen:



This is in accord with values for the ionisation potentials of amines and ethers, the energies required for excitation of a lone-pair electron being 7·84 ev for trimethylamine,[18] 9·53 ev for diethyl ether,[19] and 8·20 ev for anisole.[19] In general, alkyl halides have higher ionisation potentials than ethers and it is unlikely therefore that the reactivity of carbon–hydrogen bonds, adjacent to halogen, towards electron-accepting radicals will be appreciably enhanced by the electron-donating effect. α-Carbon chlorination and fluorination of n-butyl halides [20] is, in fact, slightly retarded by the halogen substituent.

Differences in the reactivities of $R_2N{\cdot}CR_2{\cdot}$ and $RO{\cdot}CR_2{\cdot}$ radicals when formed, notably the fact that amine radicals are longer lived, indicate that, as in the transition states for their formation, resonance stabilisation by electron donation is greater with adjacent nitrogen than with adjacent oxygen.

## Experimental

Extracts were dried over $MgSO_4$. Light petroleum (b. p. 40—60°) was used. Anisole was washed with aqueous 10% sodium hydroxide and water, and then dried and fractionated, the middle fraction of b. p. 151° being collected; its vapour-phase chromatogram (polyethylene glycol–Celite; 75°; argon) showed a single peak. t-Butyl peroxide (Laporte) was gas-chromatographically homogeneous and was used without purification.

*Decomposition of t-Butyl Peroxide in Anisole.*—Anisole (32·3 g., 10 mol.) and the peroxide (4·33 g., 1 mol.) were kept under nitrogen in a sealed tube at 140° for 60 hr. t-Butyl alcohol (2·41 g.) and acetone (1·15 g.) in the mixture were determined by vapour-phase chromatography (trixylyl phosphate–Celite, 18°, nitrogen) with propan-1-ol as internal standard. In a separate experiment, acetone and t-butyl alcohol were distilled from the reaction mixture, and acetone was characterised as the 2,4-dinitrophenylhydrazone, m. p. and mixed m. p. 125°. The mixture was washed with aqueous 5% sodium hydroxide which extracted phenol (0·105 g.) estimated as the tribromo-derivative (0·369 g.), m. p. and mixed m. p. 88°. Slow distillation up to 70°/30 mm. gave a fraction consisting of anisole containing methoxytoluenes (see below). The residue was fractionally distilled: the fore-run, b. p. 60—106°/0·2 mm., showed a carbonyl band at 1680 cm.$^{-1}$ and gave a 2,4-dinitrophenylhydrazone (0·05 g.) which, after chromatography on bentonite–kieselguhr, had m. p. 248—250°, alone or mixed with *o*-methoxybenzaldehyde 2,4-dinitrophenylhydrazone (m. p. 250°). The main fraction (0·75 g.), b. p. 108—130°/0·2 mm. (Found: C, 78·1; H, 6·7. Calc. for $C_{14}H_{14}O_2$: C, 78·5; H, 6·6%), showed an ether band at 1240 cm.$^{-1}$ and treatment with aqueous 48% hydrogen bromide gave phenol but no dibromomethane or 1,2-dibromoethane (vapour-phase chromatography).

A portion (0·8 g.) of the main fraction in ethanol (20 ml.) was hydrogenated over 5% palladised charcoal (0·22 g.). After absorption (50 ml.) had ceased, ether (100 ml.) was added and the suspension was filtered. Extraction of the filtrate with aqueous 5% sodium hydroxide gave phenol (0·06 g.) estimated as the tribromo-derivative (0·210 g.). Distillation of the ethereal solution gave a fraction (0·08 g.), b. p. 83°/25 mm., $n_D^{18}$ 1·5236, which showed *ortho-*, *meta*, and *para*-substitution in the 690—850 cm.$^{-1}$ region and the vapour-phase chromatogram (trixylyl phosphate; 130°, nitrogen) showed two peaks with the retention times of *o*- (13·4 min.) and *p*-methoxytoluene (15·5 min.), respectively. A higher yield (55%) of the methoxytoluenes was obtained by reduction of the fraction with lithium (100% excess) in liquid ammonia (Found: C, 78·55; H, 8·6. Calc. for $C_8H_{10}O$: C, 78·7; H, 8·3%).

The distillation residue (2·24 g.) was chromatographed on alumina, yielding only amorphous solids of indefinite m. p. Reductive cleavage as above gave phenol as the only identifiable product.

[18] Watanabe and Mottl, *J. Chem. Phys.*, 1957, **26**, 1773.
[19] Watanabe, *J. Chem. Phys.*, 1957, **26**, 542.
[20] Fredricks and Tedder, *J.*, 1960, 144.

In a separate experiment, the reaction mixture was distilled into three fractions of b. p. <200°: (i) 80—152°/760 mm.; (ii) 152°/760 mm.; (iii) 50°/10 mm. Each was examined by vapour-phase chromatography (trixylyl phosphate–Celite, 121°); apart from anisole, fractions (ii) and (iii) showed a peak with the retention time of *o*-methoxytoluene, possessing a shoulder (on the later side) due to the *meta*- and *para*-isomers. Owing to the relatively small sizes of these peaks, the total yield of methoxytoluenes could only approximately be estimated, at 29% ± 5% (based on acetone; dimethylaniline as internal standard).

*Anisole–Peroxide Reactions at Higher Molar Ratios.*—(i) Anisole (159 g., 50 mol.) and peroxide (4·3 g., 1 mol.) were heated at 140° for 60 hr. (reflux condenser) in a slow stream of nitrogen. After removal of the fraction containing phenol and anisole as before, distillation of the residue gave an isomeric mixture of phenoxymethylanisoles (1·48 g., 23·5%), b. p. 106—110°/0·11 mm. (ii) Repetition of Johnston and Williams's [12] experiment with anisole (108 g.) and peroxide (4 g.) at 110° for 72 hr. (reflux condenser) gave phenoxymethylanisoles (0·25 g., 4·3%), b. p. 140°/4 mm. The infrared spectrum was identical with that of the phenoxymethylanisole fractions obtained above.

o-*Phenoxymethylanisole.*—2-Methoxybenzyl chloride, b. p. 122—124°/28 mm., $n_D^{22}$ 1·5481, was obtained by treatment of 2-methoxybenzyl alcohol [21] with thionyl chloride in benzene [22] (lit.,[21] b. p. 110—114°/14 mm.). The chloride (9·9 g.) was heated under reflux for 8 hr. with phenol (6·5 g.) and a suspension of anhydrous potassium carbonate (30 g.) in acetone (40 ml.). The mixture was filtered and the residue, from evaporation of the filtrate, was washed in ether (300 ml.) with aqueous 10% sodium hydroxide, dried, and evaporated. Distillation of the residue gave recovered chloride (1·1 g.), b. p. 58—62°/0·1 mm., and then the *ether* (8·8 g.), b. p. 116—120°/0·1 mm., $n_D^{19.5}$ 1·5800 (Found: C, 78·5; H, 6·3%).

m-*Phenoxymethylanisole.*—3-Methoxybenzyl chloride [23] was treated with phenol under the above conditions, yielding the *ether* (57%), b. p. 134—136°/0·2 mm., $n_D^{18}$ 1·5790 (Found: C, 78·0; H, 6·7%).

p-*Phenoxymethylanisole.*—4-Methoxybenzyl chloride [24] was converted as before into the *ether* (58%), b. p. 124—126°/0·4 mm., m. p. 76—80°, raised to 92—92·5° (from benzene–light petroleum) (Found: C, 78·5; H, 6·6%).

*Reaction of* p-*Dimethoxybenzene with t-Butyl Peroxide.*—Reactions were carried out as for the anisole reactions with the ether (32 g.) and peroxide (3·38 g.). When reaction was complete the mixture, in chloroform (250 ml.), was extracted with aqueous 5% sodium hydroxide. Chloroform and the excess of the ether were removed and distillation of the residue gave 2,5-*dimethoxybenzyl* p-*methoxyphenyl ether* (1·2141 g.), b. p. 150—160°/0·2 mm., m. p. 50—54° raised to 62—63° (from benzene–light petroleum) (Found: C, 70·0; H, 6·8. $C_{16}H_{18}O_4$ requires C, 70·1; H, 6·6%) alone or mixed with an authentic specimen (below). Attempts to obtain recognisable products from the residue (2·2 g.), by chromatography on alumina or sodium–ammonia reduction, failed.

2,5-*Dimethoxybenzyl* p-*Methoxyphenyl Ether.*—Treatment of 2,5-dimethoxybenzoic acid [25] with methanol and sulphuric acid gave *methyl* 2,5-*dimethoxybenzoate*, b. p. 95—98°/1 mm., $n_D^{17.5}$ 1·5416 (Found: C, 60·9; H, 6·0. $C_{10}H_{12}O_4$ requires C, 61·2; H, 6·2%). Reduction of the ester (8 g.) with lithium aluminium hydride (4·5 g.) in ether (250 ml.) gave 2,5-dimethoxybenzyl alcohol (4·1 g.), b. p. 122—125°/1 mm., $n_D^{17}$ 1·5490 (lit.,[26] b. p. 85—90°/0·025 mm.), which was converted with thionyl chloride in benzene into 2,5-dimethoxybenzyl chloride, m. p. 66° (lit.,[27] 70—72°). The chloride (0·6 g.) was refluxed for 40 hr. with *p*-methoxyphenol (0·5 g.) and a suspension of potassium carbonate (10 g.) in acetone (25 ml.). The mixture was filtered and ether (100 ml.) was added to the filtrate. The excess of *p*-methoxyphenol was removed with aqueous sodium hydroxide and evaporation of the ethereal solution gave the ether (0·3 g.), m. p. 62—62·5° (from benzene–light petroleum) (Found: C, 70·3; H, 6·7%).

*Determination of the Ratios of Isomeric Phenoxymethylanisoles from the Anisole–Peroxide Reaction.*—Duplicate experiments were carried out as previously described except that in

[21] Cragoe and Pietrusykiewicz, *J. Org. Chem.*, 1957, **22**, 1338.
[22] Newman, *J. Amer. Chem. Soc.*, 1940, **62**, 2295.
[23] Tsukamoto, Yoshimura, and Toki, *Pharm. Bull.* (*Japan*), 1955, **3**, 239.
[24] Quelet, *Compt. rend.*, 1934, **198**, 102.
[25] Graebe and Martz, *Annalen*, 1905, **340**, 213.
[26] Shulgin and Gal, *J.*, 1953, 1316.
[27] Harley-Mason and Jackson, *J.*, 1954, 1165.

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addition the reaction mixtures were extracted with saturated aqueous sodium hydrogen sulphite to remove aldehydes. The yields of phenoxymethylanisoles were 0·78 g. and 0·72 g., respectively [Found: (i) C, 78·2; H, 6·2; (ii) C, 78·1; H, 6·8%]. Vapour-phase chromatography (7% polyphenyl ether–Celite at 183°; argon) of the isomeric mixtures gave complete resolution of the isomers and peak areas were measured with a planimeter. The area–concentration dependence was checked with mixtures of the individual isomers of known compositions.

TABLE 1.

Isomer ratio determinations on mixtures of phenoxymethyl anisoles.

| | Found (%) | | | Known (%) | | |
|---|---|---|---|---|---|---|
| | *o*- | *m*- | *p*- | *o*- | *m*- | *p*- |
| Expt. (i) | 69 | 22 | 9 | — | — | — |
| Expt. (ii) | 71 | 20 | 9 | — | — | — |
| Synthetic mixture (i) | 74 | 20 | 6 | 75·5 | 19·2 | 6·3 |
| Synthetic mixture (ii) | 68 | 24·7 | 7·3 | 69 | 23 | 8 |

*Photochemical Decomposition of t-Butyl Peroxide in Anisole.*—t-Butyl peroxide (4·32 g.) in anisole (32·1 g.), contained in a quartz flask, was irradiated with a Hanovia mercury arc lamp type 590/10 (principal wavelength of emission 2570 Å), the temperature of the solution being kept at 40—45°. After 96 hr., decomposed peroxide, t-butyl alcohol, and anisole were distilled off. The distillate was shown to contain 70% of the original peroxide and the absence of acetone was established by vapour-phase chromatography (trixylyl phosphate–Celite; 18°; nitrogen). The higher-boiling fraction, in benzene, was washed with aqueous 5% sodium hydroxide and, after removal of the solvent, distillation of the residue gave a fraction (0·24 g.), b. p. 125°/0·3 mm., m. p. 25—40°. 1,2-Diphenoxyethane (0·21 g.) and phenoxymethylanisoles (43 mg., essentially the *ortho*-isomer) in this fraction were determined by vapour-phase chromatography (polyphenyl ether–Celite; 183°; argon). The distillation residue (0·55 g.) was not further investigated. In another experiment, the "dimer" fraction was crystallised from ethanol, to give 1,2-diphenoxyethane, m. p. and mixed m. p. 97°, with an infrared spectrum identical with that of an authentic sample.

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## 1037. *The Crystal Structure of Monopyridinecopper(II) Acetate.*

By G. A. BARCLAY and C. H. L. KENNARD.

The structure of monopyridinecopper(II) acetate has been determined by Patterson and Fourier syntheses from three-dimensional *X*-ray diffraction spectra. The copper atoms are bridged in pairs by four acetate groups to form binuclear molecules, $Cu_2(CH_3{\cdot}CO_2)_4,2C_5H_5N$, similar to those found in copper acetate monohydrate. The copper atom is 0·22 Å out of the plane of the four oxygen atoms to which it is joined by covalent bonds (1·98 Å in length). The nitrogen atom of a pyridine molecule is attached to the copper atom by a slightly elongated covalent bond (2·13 Å long), giving the copper atom a distorted tetragonal-pyramidal co-ordination. The sixth, "octahedral," site is occupied by the second copper atom to which a δ-bond is formed (Cu–Cu distance 2·63 Å). The binuclear molecule as a whole possesses a two-fold axis of symmetry which passes through the copper atoms and the pyridine molecules.

COPPER ACETATE MONOHYDRATE is a binuclear molecule, $Cu_2(CH_3{\cdot}CO_2)_4,2H_2O$, in which the copper atoms are bridged in pairs by four acetate groups.[1] The close approach of

[1] van Niekerk and Shoening, *Acta Cryst.*, 1953, **6**, 227.

the two copper atoms (2·64 Å) is consistent with the formation of a δ-bond between them.[2,3] The low magnetic moment at room temperature ($\mu = 1{\cdot}40$ B.M.) and the antiferromagnetic behaviour in the variation of magnetic susceptibility with temperature are considered to result from the binuclear molecules.[3] On the basis of magnetic susceptibility, absorption spectra, and other physical quantities, several simple and complex copper alkanoates are claimed to have similar binuclear molecules.[4] The structure of one such compound, monopyridinecopper(II) acetate, has now been determined.

## Experimental

Monopyridinecopper(II) acetate, in the form of dark-green acicular crystals, was supplied by Dr. R. L. Martin and Miss H. Waterman. Oscillation and Weissenberg photographs showed them to be monoclinic. Systematically absent spectra (*hkl* with $h + 1 = 2n + 1$; *h0l* with $h = 2n + 1$) indicated that the space group was either $Aa$ or $A2/a$. Accurate cell dimensions were determined from photographs taken on a Guinier focusing powder camera. The intensities of 1200 independent reflections were estimated visually from equi-inclination Weissenberg photographs by the multiple-film technique. The usual Lorentz and polarisation factors were applied to the intensities of the observed reflections; no allowance was made for absorption or extinction. The resulting intensities were correlated so that all observed data were on the same relative scale. The observed structure amplitudes were placed on an absolute scale by comparison with the calculated values.

*Crystal Data.*—$Cu(CH_3{\cdot}CO_2)_2C_5H_5N$; $M = 265{\cdot}64$; monoclinic; $a = 12{\cdot}542 \pm 0{\cdot}010$, $b = 17{\cdot}314 \pm 0{\cdot}010$, $c = 9{\cdot}955 \pm 0{\cdot}005$ Å, $\beta = 96°\ 43' \pm 10'$; $U = 2144$ Å$^3$; $D_m = 1{\cdot}62 \pm 0{\cdot}01$ g. cm.$^{-3}$ (by flotation); $Z = 8$; $D_c = 1{\cdot}615$ g. cm.$^{-3}$; $F(000) = 1064$; space group, $A2/a$ ($C_{2h}^6$, No. 15); radiation, copper, unfiltered; single-crystal oscillation and Weissenberg photographs; data for structure analysis from *hk*0 ⟶ *hk*7, *h*0*l* ⟶ *h*8*l*.

*Structure Determination.*—A statistical analysis of the 1200 three-dimensional intensities by the method of Howells, Phillips, and Rogers [5] indicated that the space group was probably centrosymmetric. Hence, the space group $A2/a$ was assumed and was confirmed by the subsequent satisfactory refinement.

There is no requirement for any atom to be in special positions in the unit cell as there are eight equivalent general positions whose fractional co-ordinates are $\pm(x,y,z;\ \frac{1}{2}+x,\bar{y},z;\ x,\frac{1}{2}+y,\frac{1}{2}+z;\ \frac{1}{2}+x,\frac{1}{2}-y,\frac{1}{2}+z)$. However, if the structure is similar to that of copper acetate monohydrate, the binuclear unit must possess a two-fold axis of rotation or a centre of symmetry.

A three-dimensional Patterson function was interpreted to indicate that the copper atoms

Table 1.

Atomic parameters.

| Atom | *x/a* | *y/b* | *z/c* | σ (Å) | Atom | *x/a* | *y/b* | *z/c* | σ (Å) |
|---|---|---|---|---|---|---|---|---|---|
| Cu(1) ... | 0·2500 | 0·0529 | 0·0000 | 0·002 | C(4) ..... | 0·2244 | 0·4488 | 0·1126 | 0·014 |
| Cu(2) ... | 0·2500 | 0·2049 | 0·0000 | 0·002 | C(5) ..... | 0·0395 | 0·1278 | 0·2801 | 0·019 |
| O(1) ..... | 0·3621 | 0·1906 | 0·1558 | 0·011 | C(6) ..... | 0·4857 | 0·1278 | 0·3116 | 0·019 |
| O(2) ..... | 0·1404 | 0·1923 | 0·1272 | 0·010 | C(7) ..... | 0·3484 | −0·1921 | −0·0203 | 0·016 |
| O(3) ..... | 0·1500 | 0·0657 | 0·1391 | 0·010 | C(8) ..... | 0·3420 | −0·1108 | −0·0161 | 0·011 |
| O(4) ..... | 0·3719 | 0·0645 | 0·1431 | 0·010 | C(9) ..... | 0·2500 | −0·2302 | 0·0000 | 0·014 |
| C(1) ..... | 0·4012 | 0·1274 | 0·1962 | 0·011 | C(10) ... | 0·2500 | 0·4916 | 0·0000 | 0·012 |
| C(2) ..... | 0·1157 | 0·1291 | 0·1694 | 0·018 | N(1) ... | 0·2500 | −0·0696 | 0·0000 | 0·009 |
| C(3) ..... | 0·2234 | 0·3691 | 0·1096 | 0·012 | N(2) ... | 0·2500 | 0·3279 | 0·0000 | 0·011 |

were not in general positions but lay on the two-fold axes in two independent sets of special positions of the type $\pm(\frac{1}{4},y,0;\ \frac{1}{4},\frac{1}{2}+y,\frac{1}{2})$. Structure factors were calculated with $y_1 = 0{\cdot}056$ and $y_2 = 0{\cdot}202$ for the two copper atoms; the $R$ factor was 0·40. This interpretation of the Patterson map strongly suggests the binuclear arrangement, in which case the nitrogen atom

[2] Figgis and Martin, *J.*, 1956, 3837.
[3] Ross, *Trans. Faraday Soc.*, 1959, **55**, 1057.
[4] Martin and Waterman, *J.*, 1957, 2545; Martin and Whitley, *J.*, 1958, 1394; Martin and Waterman, *J.*, 1959, 1359; Graddon, *Nature*, 1960, **186**, 715.
[5] Howells, Phillips, and Rogers, *Acta Cryst.*, 1950, **3**, 210.

TABLE 2.

Calculated structure factors and observed structure amplitudes. (Scale: $\frac{1}{5}$ absolute values.)

| $l$ | $F_c$ | $\lvert F_o\rvert$ |
|---|---|---|
| | 0,0,$l$ | |
| 2 | 53 | 56 |
| 4 | 22 | 27 |
| 6 | 57 | 59 |
| 8 | 34 | 31 |
| 10 | 17 | 15 |
| 12 | 9 | 9 |
| | 0,1,$l$ | |
| 1 | 54 | 49 |
| 3 | 12 | 19 |
| 5 | 27 | 28 |
| 7 | 28 | 28 |
| 9 | 7 | 6 |
| 11 | 6 | 5 |
| | 0,2,$l$ | |
| 0 | −2 | 4 |
| 2 | −4 | 6 |
| 4 | −8 | 10 |
| 6 | −3 | 4 |
| | 0,3,$l$ | |
| 3 | −1 | 5 |
| 5 | −7 | 9 |
| 7 | −9 | 10 |
| | 0,4,$l$ | |
| 0 | −29 | 28 |
| 2 | 34 | 38 |
| 4 | 11 | 13 |
| 6 | 5 | 5 |
| 8 | 10 | 12 |
| | 0,5,$l$ | |
| 1 | 22 | 24 |
| 3 | 4 | 4 |
| 5 | 7 | 5 |
| 7 | 9 | 10 |
| 9 | 8 | 8 |
| | 0,6,$l$ | |
| 0 | −6 | 8 |
| 2 | −6 | 10 |
| 6 | −4 | 5 |
| 8 | −4 | 6 |
| | 0,7,$l$ | |
| 1 | −61 | 58 |
| 3 | −20 | 22 |
| 5 | −23 | 28 |
| 7 | −27 | 28 |
| 9 | −15 | 13 |
| 11 | −6 | 4 |
| | 0,8,$l$ | |
| 0 | −43 | 45 |
| 2 | −36 | 35 |
| 4 | −4 | 3 |
| 6 | −23 | 25 |
| 8 | −22 | 22 |
| | 0,9,$l$ | |
| 1 | −9 | 10 |
| 3 | 5 | 8 |
| 7 | −6 | 8 |
| | 0,10,$l$ | |
| 0 | 1 | 4 |
| 2 | 5 | 7 |
| 4 | 5 | 7 |
| | 0,11,$l$ | |
| 1 | −6 | 7 |
| 3 | −17 | 18 |
| 5 | −15 | 18 |
| 7 | −7 | 9 |
| 9 | −3 | 3 |
| | 0,12,$l$ | |
| 0 | −36 | 37 |
| 2 | −13 | 14 |
| 4 | −13 | 13 |
| 6 | −14 | 14 |
| 8 | −9 | 7 |
| 10 | −9 | 7 |

| $l$ | $F_c$ | $\lvert F_o\rvert$ |
|---|---|---|
| | 0,13,$l$ | |
| 1 | −15 | 17 |
| 3 | −10 | 11 |
| 5 | −11 | 13 |
| 7 | −8 | 9 |
| | 0,14,$l$ | |
| 0 | 10 | 13 |
| 6 | 5 | 7 |
| 8 | 4 | 4 |
| | 0,15,$l$ | |
| 1 | 17 | 20 |
| 3 | 4 | 5 |
| 5 | 10 | 11 |
| 7 | 11 | 11 |
| 9 | 4 | 3 |
| | 0,16, | |
| 0 | 22 | 25 |
| 4 | −2 | 4 |
| 6 | 7 | 8 |
| 8 | 4 | 4 |
| | 0,17,$l$ | |
| 3 | −3 | 5 |
| 7 | 1 | 3 |
| | 0,18,$l$ | |
| 2 | 6 | 6 |
| 4 | 8 | 6 |
| 6 | 3 | 4 |
| | 0,19,$l$ | |
| 1 | 9 | 9 |
| 3 | 12 | 11 |
| 5 | 8 | 6 |
| | 0,20,$l$ | |
| 0 | 7 | 8 |
| 2 | 11 | 10 |
| 4 | 7 | 5 |
| | 0,21,$l$ | |
| 1 | 2 | 3 |
| 3 | 2 | 3 |
| | 0,22,$l$ | |
| 0 | −2 | 2 |
| | 1,1,$l$ | |
| −11 | −7 | 6 |
| −9 | −10 | 8 |
| −7 | −28 | 27 |
| −5 | −11 | 12 |
| −3 | 14 | 19 |
| −1 | −50 | 45 |
| 1 | −45 | 46 |
| 3 | 10 | 17 |
| 5 | −11 | 14 |
| 7 | −14 | 14 |
| | 1,2,$l$ | |
| −12 | −5 | 3 |
| −10 | −5 | 5 |
| −8 | −6 | 6 |
| −6 | −27 | 30 |
| −2 | 13 | 16 |
| 0 | −34 | 44 |
| 2 | 14 | 15 |
| 6 | −16 | 20 |
| | 1,3,$l$ | |
| −7 | −6 | 7 |
| −5 | 5 | 7 |
| −3 | 16 | 18 |
| −1 | −20 | 22 |
| 1 | −19 | 19 |
| 3 | 16 | 16 |
| | 1,4,$l$ | |
| −4 | −9 | 10 |
| −2 | −8 | 9 |
| | 1,5,$l$ | |
| −9 | −10 | 8 |
| −7 | −13 | 13 |

| $l$ | $F_c$ | $\lvert F_o\rvert$ |
|---|---|---|
| −5 | −10 | 11 |
| −3 | −13 | 12 |
| −1 | −24 | 24 |
| 1 | −24 | 24 |
| 3 | −13 | 14 |
| 5 | −10 | 10 |
| 7 | −16 | 16 |
| | 1,6,$l$ | |
| −12 | −7 | 5 |
| −10 | −7 | 4 |
| −8 | −26 | 22 |
| −6 | −24 | 25 |
| −4 | −12 | 9 |
| −2 | −38 | 36 |
| 0 | −46 | 35 |
| 2 | −32 | 30 |
| 4 | −18 | 20 |
| 6 | −25 | 26 |
| 8 | −17 | 20 |
| 10 | −12 | 12 |
| | 1,7,$l$ | |
| −9 | −12 | 10 |
| −7 | −20 | 21 |
| −5 | −15 | 18 |
| −3 | −15 | 17 |
| −1 | −39 | 40 |
| 1 | −38 | 39 |
| 3 | −18 | 19 |
| 5 | −15 | 20 |
| 7 | −17 | 20 |
| 9 | −9 | 11 |
| 11 | −6 | 6 |
| | 1,8,$l$ | |
| −8 | 5 | 5 |
| −4 | −3 | 3 |
| 0 | 9 | 11 |
| 2 | 3 | 3 |
| 4 | −3 | 5 |
| | 1,9,$l$ | |
| −9 | 5 | 4 |
| −7 | 11 | 11 |
| −5 | 5 | 6 |
| −1 | 13 | 13 |
| 1 | 10 | 10 |
| 5 | 4 | 6 |
| 7 | 8 | 12 |
| | 1,10,$l$ | |
| −10 | −4 | 4 |
| −8 | 6 | 6 |
| −4 | −14 | 15 |
| 0 | 6 | 9 |
| 4 | −10 | 12 |
| | 1,11,$l$ | |
| −7 | −4 | 4 |
| −5 | −6 | 7 |
| −3 | −5 | 7 |
| −1 | −4 | 5 |
| 1 | −3 | 4 |
| 3 | −5 | 7 |
| 5 | −4 | 6 |
| 9 | −3 | 4 |
| | 1,12,$l$ | |
| −6 | 5 | 7 |
| −4 | 9 | 10 |
| −2 | 8 | 8 |
| 0 | 8 | 9 |
| 2 | 8 | 9 |
| 4 | 9 | 11 |
| 6 | 9 | 11 |
| 8 | 5 | 6 |
| | 1,13,$l$ | |
| −9 | 8 | 5 |
| −7 | 14 | 12 |
| −5 | 12 | 10 |
| −3 | 9 | 9 |
| −1 | 25 | 24 |
| 1 | 26 | 27 |
| 3 | 11 | 11 |
| 5 | 12 | 12 |

| $l$ | $F_c$ | $\lvert F_o\rvert$ |
|---|---|---|
| 7 | 12 | 13 |
| 9 | 10 | 10 |
| | 1,14,$l$ | |
| −8 | 9 | 7 |
| −6 | 19 | 16 |
| −4 | 14 | 13 |
| −2 | 14 | 16 |
| 0 | 24 | 26 |
| 2 | 13 | 15 |
| 4 | 14 | 17 |
| 6 | 15 | 20 |
| 8 | 9 | 11 |
| | 1,15,$l$ | |
| −9 | 3 | 2 |
| −7 | 6 | 6 |
| −5 | −2 | 4 |
| −1 | 8 | 9 |
| 1 | 7 | 8 |
| | 1,16,$l$ | |
| 0 | −6 | 7 |
| | 1,17,$l$ | |
| −5 | 4 | 4 |
| −3 | 9 | 10 |
| 3 | 8 | 10 |
| 5 | 4 | 4 |
| | 1,18,$l$ | |
| −6 | 5 | 4 |
| −4 | 11 | 11 |
| −2 | 12 | 11 |
| 0 | 6 | 7 |
| 2 | 12 | 14 |
| 4 | 10 | 12 |
| 6 | 6 | 6 |
| | 1,19,$l$ | |
| −3 | 4 | 3 |
| 1 | 3 | 4 |
| 5 | 4 | 4 |
| | 1,20,$l$ | |
| −4 | −3 | 3 |
| −2 | −5 | 5 |
| 0 | −4 | 5 |
| 2 | −4 | 5 |
| 4 | −3 | 3 |
| | 1,21,$l$ | |
| −3 | −7 | 6 |
| −1 | −7 | 7 |
| 1 | −7 | 8 |
| 3 | −6 | 6 |
| | 1,22,$l$ | |
| 0 | −3 | 4 |
| | 2,0,$l$ | |
| −12 | −8 | 6 |
| −10 | −14 | 11 |
| −8 | −31 | 31 |
| −6 | −41 | 48 |
| −4 | −22 | 25 |
| −2 | −79 | 97 |
| 0 | −87 | 75 |
| 2 | −98 | 101 |
| 4 | −48 | 54 |
| 6 | −29 | 34 |
| 8 | −33 | 52 |
| | 2,1,$l$ | |
| −11 | −6 | 4 |
| −9 | −6 | 6 |
| −7 | −14 | 15 |
| −5 | −28 | 29 |
| −3 | −23 | 22 |
| −1 | −29 | 30 |
| 1 | −25 | 25 |
| 3 | −26 | 24 |
| 5 | −32 | 33 |
| 7 | −15 | 15 |
| | 2,2,$l$ | |
| 0 | −5 | 6 |

| $l$ | $F_c$ | $\lvert F_o\rvert$ |
|---|---|---|
| 4 | 9 | 8 |
| | 2,3,$l$ | |
| −5 | 5 | 7 |
| −3 | −7 | 9 |
| −1 | 9 | 11 |
| 1 | 12 | 15 |
| 5 | 10 | 13 |
| | 2,4,$l$ | |
| −8 | −8 | 7 |
| −6 | −10 | 11 |
| −4 | −22 | 25 |
| −2 | −6 | 3 |
| 0 | −30 | 30 |
| 2 | 2 | 6 |
| 4 | −16 | 16 |
| 6 | −14 | 12 |
| | 2,5,$l$ | |
| −9 | −7 | 6 |
| −7 | −13 | 12 |
| −3 | −7 | 8 |
| −1 | −15 | 15 |
| 1 | −13 | 11 |
| 3 | −16 | 15 |
| 5 | −7 | 7 |
| 7 | −6 | 6 |
| 9 | −6 | 5 |
| 11 | −6 | 7 |
| | 2,6,$l$ | |
| −4 | 6 | 4 |
| −2 | 4 | 5 |
| 0 | 8 | 6 |
| 2 | 3 | 4 |
| 6 | 4 | 5 |
| 12 | 1 | 2 |
| | 2,7,$l$ | |
| −11 | 7 | 4 |
| −9 | 14 | 10 |
| −7 | 25 | 24 |
| −5 | 21 | 23 |
| −3 | 32 | 30 |
| −1 | 44 | 41 |
| 1 | 41 | 39 |
| 3 | 36 | 35 |
| 5 | 25 | 26 |
| 7 | 19 | 19 |
| 9 | 13 | 11 |
| | 2,8,$l$ | |
| −10 | 6 | 5 |
| −8 | 17 | 13 |
| −6 | 20 | 21 |
| −4 | 19 | 18 |
| −2 | 20 | 20 |
| 0 | 44 | 38 |
| 2 | 19 | 19 |
| 4 | 21 | 23 |
| 8 | 8 | 7 |
| 10 | 12 | 10 |
| | 2,9,$l$ | |
| −7 | 6 | 6 |
| −3 | 7 | 7 |
| −1 | 6 | 7 |
| 3 | 4 | 4 |
| 5 | 4 | 6 |
| 7 | 3 | 4 |
| | 2,10,$l$ | |
| 4 | −7 | 8 |
| 6 | −3 | 5 |
| | 2,11,$l$ | |
| −9 | 5 | 3 |
| −7 | 5 | 5 |
| −5 | 18 | 17 |
| −3 | 19 | 19 |
| −1 | 11 | 12 |
| 1 | 10 | 9 |
| 3 | 11 | 12 |
| 5 | 14 | 15 |
| 7 | 8 | 10 |
| 9 | 4 | 5 |

| $l$ | $F_c$ | $\lvert F_o\rvert$ |
|---|---|---|
| | 2,12,$l$ | |
| −10 | 7 | 5 |
| −8 | 10 | 8 |
| −6 | 12 | 11 |
| −4 | 9 | 8 |
| −2 | 19 | 19 |
| 0 | 17 | 17 |
| 2 | 24 | 23 |
| 4 | 12 | 12 |
| 6 | 8 | 7 |
| 8 | 13 | 11 |
| 10 | 7 | 6 |
| | 2,13,$l$ | |
| −7 | 5 | 6 |
| −5 | 8 | 9 |
| −3 | 7 | 8 |
| −1 | 10 | 11 |
| 1 | 9 | 10 |
| 3 | 11 | 12 |
| 5 | 11 | 12 |
| 7 | 6 | 6 |
| 9 | 6 | 5 |
| | 2,14,$l$ | |
| −8 | −4 | 4 |
| −6 | −5 | 6 |
| −4 | −6 | 5 |
| −2 | −7 | 7 |
| 0 | −6 | 8 |
| 2 | −7 | 11 |
| 6 | −3 | 4 |
| 8 | −4 | 5 |
| | 2,15,$l$ | |
| −9 | −4 | 3 |
| −7 | −8 | 7 |
| −5 | −11 | 12 |
| −3 | −9 | 9 |
| −1 | −12 | 13 |
| 1 | −11 | 12 |
| 3 | −10 | 12 |
| 5 | −10 | 13 |
| 7 | −7 | 7 |
| | 2,16,$l$ | |
| −8 | −3 | 3 |
| −2 | −6 | 6 |
| 0 | −5 | 7 |
| 2 | −8 | 8 |
| 4 | −3 | 4 |
| 6 | −1 | 3 |
| | 2,18,$l$ | |
| −4 | −5 | 5 |
| −2 | −5 | 5 |
| 0 | −6 | 6 |
| 2 | −4 | 5 |
| 4 | −4 | 5 |
| 6 | −4 | 6 |
| | 2,19,$l$ | |
| 1 | −10 | 9 |
| 3 | −9 | 9 |
| 5 | −8 | 8 |
| | 2,20,$l$ | |
| −4 | −7 | 5 |
| −2 | −7 | 7 |
| 0 | −10 | 9 |
| 2 | −7 | 6 |
| 4 | −8 | 7 |
| | 2,21,$l$ | |
| −3 | −2 | 2 |
| 3 | −2 | 6 |
| | 3,1,$l$ | |
| −11 | 8 | 5 |
| −9 | 17 | 12 |
| −7 | 18 | 15 |
| −5 | 25 | 27 |
| −3 | 36 | 35 |
| −1 | 20 | 21 |
| 1 | 27 | 30 |
| 3 | 44 | 45 |
| 5 | 11 | 9 |

XUM

TABLE 2. (*Continued.*)

| *l* | $F_c$ | $\lvert F_o\rvert$ |
|---|---|---|
| | 3,2,*l* | |
| −12 | 8 | 5 |
| −8 | 12 | 10 |
| −6 | 13 | 12 |
| −4 | 33 | 37 |
| −2 | 42 | 42 |
| 0 | −34 | 45 |
| 2 | 27 | 24 |
| 4 | 29 | 30 |
| | 3,3,*l* | |
| −9 | 5 | 5 |
| −5 | 2 | 4 |
| −3 | 3 | 3 |
| −1 | −2 | 2 |
| 1 | 11 | 13 |
| 3 | 10 | 12 |
| 5 | −8 | 12 |
| | 3,4,*l* | |
| −4 | 7 | 9 |
| 0 | −3 | 5 |
| 4 | 1 | 4 |
| 6 | 5 | 6 |
| | 3,5,*l* | |
| −11 | 6 | 4 |
| −7 | 9 | 10 |
| −5 | 12 | 13 |
| −3 | 13 | 14 |
| −1 | 13 | 13 |
| 1 | 14 | 13 |
| 3 | 13 | 14 |
| 5 | 16 | 19 |
| 7 | 7 | 6 |
| 9 | 7 | 7 |
| 11 | 7 | 6 |
| | 3,6,*l* | |
| −12 | 7 | 4 |
| −10 | 13 | 9 |
| −8 | 13 | 10 |
| −6 | 23 | 22 |
| −4 | 34 | 30 |
| −2 | 21 | 20 |
| 0 | 35 | 31 |
| 2 | 25 | 24 |
| 4 | 36 | 37 |
| 6 | 18 | 22 |
| 8 | 9 | 8 |
| 10 | 13 | 13 |
| | 3,7,*l* | |
| −11 | 6 | 5 |
| −9 | 9 | 6 |
| −7 | 15 | 14 |
| −5 | 18 | 21 |
| −3 | 24 | 24 |
| −1 | 24 | 24 |
| 1 | 21 | 22 |
| 3 | 27 | 29 |
| 5 | 21 | 23 |
| 7 | 7 | 8 |
| 9 | 9 | 10 |
| 11 | 8 | 8 |
| | 3,8,*l* | |
| −6 | −6 | 6 |
| −4 | −4 | 7 |
| −2 | −4 | 4 |
| 0 | −9 | 12 |
| 2 | −7 | 9 |
| 4 | −4 | 5 |
| 10 | −2 | 3 |
| | 3,9,*l* | |
| −7 | −8 | 7 |
| −5 | −12 | 12 |
| −3 | −16 | 16 |
| −1 | −7 | 6 |
| 3 | −13 | 14 |
| 5 | −14 | 16 |
| 7 | 1 | 6 |
| | 3,10,*l* | |
| −8 | 3 | 5 |
| −2 | 10 | 13 |
| 2 | 5 | 6 |
| 4 | −1 | 4 |
| 6 | 4 | 6 |
| 8 | 5 | 8 |

| *l* | $F_c$ | $\lvert F_o\rvert$ |
|---|---|---|
| | 3,11,*l* | |
| −9 | 6 | 5 |
| −7 | 8 | 6 |
| −5 | 8 | 8 |
| −3 | 9 | 11 |
| −1 | 10 | 11 |
| 1 | 9 | 10 |
| 3 | 8 | 9 |
| 5 | 3 | 4 |
| 7 | 4 | 5 |
| | 3,12,*l* | |
| −4 | −6 | 8 |
| −2 | −4 | 6 |
| 2 | −5 | 6 |
| 4 | −5 | 8 |
| 6 | −6 | 8 |
| 8 | −4 | 5 |
| | 3,13,*l* | |
| −9 | −10 | 6 |
| −7 | −10 | 8 |
| −5 | −12 | 10 |
| −3 | −15 | 15 |
| −1 | −14 | 12 |
| 1 | −19 | 18 |
| 3 | −20 | 22 |
| 5 | −8 | 8 |
| 7 | −9 | 9 |
| 9 | −10 | 7 |
| | 3,14,*l* | |
| −8 | −11 | 7 |
| −6 | −13 | 12 |
| −4 | −22 | 20 |
| −2 | −24 | 22 |
| 0 | −8 | 9 |
| 2 | −20 | 21 |
| 4 | −20 | 23 |
| 6 | −10 | 12 |
| 8 | −8 | 8 |
| | 3,15,*l* | |
| −9 | −5 | 4 |
| −7 | −5 | 4 |
| −5 | −4 | 4 |
| −3 | −6 | 8 |
| −1 | −5 | 6 |
| 1 | −6 | 6 |
| 3 | −7 | 9 |
| | 3,16,*l* | |
| 2 | 4 | 5 |
| 4 | 2 | 4 |
| | 3,17,*l* | |
| −1 | −6 | 7 |
| 1 | −5 | 6 |
| 5 | −5 | 6 |
| | 3,18,*l* | |
| −6 | −8 | 6 |
| −4 | −7 | 7 |
| −2 | −7 | 8 |
| 0 | −14 | 15 |
| 2 | −7 | 9 |
| 4 | −7 | 8 |
| | 3,19,*l* | |
| −1 | −4 | 4 |
| 1 | −4 | 4 |
| | 3,20,*l* | |
| −4 | 4 | 3 |
| −2 | 3 | 3 |
| 0 | 5 | 5 |
| 2 | 4 | 4 |
| 4 | 3 | 4 |
| | 4,0,*l* | |
| −12 | 8 | 5 |
| −10 | 17 | 17 |
| −8 | 22 | 24 |
| −6 | 17 | 18 |
| −4 | 59 | 74 |
| −2 | 39 | 39 |

| *l* | $F_c$ | $\lvert F_o\rvert$ |
|---|---|---|
| 0 | 17 | 26 |
| 2 | 71 | 63 |
| 4 | 57 | 55 |
| 6 | 14 | 14 |
| 8 | 17 | 14 |
| 10 | 22 | 15 |
| | 4,1,*l* | |
| −11 | 7 | 5 |
| −9 | 8 | 6 |
| −5 | 19 | 18 |
| −3 | 52 | 48 |
| −1 | −10 | 12 |
| 1 | −10 | 17 |
| 3 | 47 | 48 |
| 5 | 16 | 12 |
| | 4,2,*l* | |
| −2 | −3 | 3 |
| 0 | 9 | 9 |
| 2 | 7 | 7 |
| | 4,3,*l* | |
| −5 | 8 | 9 |
| −3 | −14 | 16 |
| −1 | 16 | 17 |
| 1 | 18 | 21 |
| 3 | −17 | 21 |
| | 4,4,*l* | |
| −12 | 5 | 3 |
| −10 | 6 | 5 |
| −6 | 18 | 18 |
| −4 | 14 | 13 |
| −2 | 23 | 24 |
| 0 | 18 | 15 |
| 2 | 12 | 13 |
| 4 | 14 | 14 |
| | 4,5,*l* | |
| −11 | 5 | 3 |
| −9 | 6 | 4 |
| −7 | 7 | 8 |
| −5 | 12 | 14 |
| −3 | 6 | 8 |
| −1 | 12 | 10 |
| 1 | 12 | 10 |
| 3 | 9 | 10 |
| 5 | 14 | 14 |
| 9 | 6 | 6 |
| 11 | 5 | 4 |
| | 4,6,*l* | |
| −6 | −4 | 4 |
| −4 | −7 | 7 |
| −2 | −2 | 4 |
| 0 | −4 | 3 |
| 2 | −7 | 7 |
| 4 | −4 | 6 |
| 8 | −2 | 4 |
| | 4,7,*l* | |
| −11 | −12 | 7 |
| −9 | −11 | 8 |
| −7 | −12 | 10 |
| −5 | −33 | 35 |
| −3 | −34 | 36 |
| −1 | −22 | 23 |
| 1 | −29 | 30 |
| 3 | −36 | 37 |
| 5 | −28 | 29 |
| 7 | −8 | 7 |
| 9 | −13 | 13 |
| 11 | −10 | 10 |
| | 4,8,*l* | |
| −10 | −12 | 9 |
| −8 | −6 | 4 |
| −6 | −17 | 20 |
| −4 | −33 | 33 |
| −2 | −26 | 25 |
| 0 | −4 | 3 |
| 2 | −29 | 26 |
| 4 | −33 | 33 |
| 6 | −9 | 11 |
| 8 | −9 | 10 |
| 10 | −11 | 10 |
| | 4,9,*l* | |
| −11 | −5 | 3 |
| −5 | −13 | 14 |

| *l* | $F_c$ | $\lvert F_o\rvert$ |
|---|---|---|
| −3 | −12 | 13 |
| 3 | −10 | 11 |
| 5 | −9 | 12 |
| 7 | 2 | 5 |
| 9 | −3 | 3 |
| | 4,10,*l* | |
| −8 | −4 | 4 |
| 0 | −10 | 11 |
| 2 | −7 | 7 |
| | 4,11,*l* | |
| −9 | −7 | 5 |
| −7 | −9 | 7 |
| −5 | −11 | 12 |
| −3 | −22 | 22 |
| −1 | −16 | 16 |
| 1 | −11 | 12 |
| 3 | −15 | 15 |
| 5 | −9 | 11 |
| 7 | −12 | 15 |
| 9 | −4 | 4 |
| | 4,12,*l* | |
| −8 | −12 | 9 |
| −6 | −8 | 6 |
| −4 | −11 | 12 |
| −2 | −12 | 14 |
| 0 | −15 | 15 |
| 2 | −17 | 18 |
| 4 | −11 | 15 |
| 6 | −8 | 9 |
| 8 | −8 | 7 |
| | 4,13,*l* | |
| −5 | −2 | 5 |
| −3 | −10 | 10 |
| 3 | −10 | 12 |
| 5 | −6 | 7 |
| 7 | −5 | 7 |
| 9 | −3 | 4 |
| | 4,14,*l* | |
| −8 | 4 | 3 |
| −6 | 6 | 6 |
| −4 | 10 | 11 |
| −2 | 8 | 9 |
| 0 | 7 | 7 |
| 2 | 10 | 11 |
| 4 | 7 | 9 |
| 6 | 3 | 4 |
| 8 | 3 | 4 |
| | 4,15,*l* | |
| −5 | 9 | 9 |
| −3 | 19 | 19 |
| 1 | 4 | 4 |
| 3 | 18 | 20 |
| 5 | 7 | 10 |
| 7 | 5 | 5 |
| | 4,16,*l* | |
| −4 | 6 | 7 |
| 0 | −3 | 6 |
| 2 | 7 | 8 |
| 4 | 6 | 9 |
| 6 | −1 | 3 |
| | 4,17,*l* | |
| −7 | −3 | 3 |
| −1 | −5 | 6 |
| 1 | −4 | 6 |
| | 4,18,*l* | |
| −6 | 4 | 3 |
| −4 | 3 | 3 |
| −2 | 4 | 4 |
| 0 | 6 | 8 |
| 2 | 4 | 5 |
| 4 | 3 | 3 |
| | 4,19,*l* | |
| −5 | 9 | 6 |
| −3 | 6 | 4 |
| −1 | 11 | 9 |
| 1 | 11 | 10 |
| 3 | 6 | 5 |
| | 4,20,*l* | |
| −4 | 6 | 4 |

| *l* | $F_c$ | $\lvert F_o\rvert$ |
|---|---|---|
| −2 | 7 | 6 |
| 0 | 8 | 6 |
| 2 | 7 | 6 |
| 4 | 7 | 7 |
| | 5,1,*l* | |
| −11 | −8 | 4 |
| −9 | −13 | 8 |
| −7 | −13 | 12 |
| −5 | −22 | 19 |
| −3 | −48 | 53 |
| −1 | −16 | 14 |
| 1 | −24 | 23 |
| 3 | −46 | 42 |
| 5 | −18 | 15 |
| | 5,2,*l* | |
| −10 | −11 | 6 |
| −6 | −5 | 5 |
| −4 | −51 | 43 |
| −2 | −23 | 22 |
| 0 | 0 | 3 |
| 2 | −21 | 22 |
| 4 | −30 | 26 |
| | 5,3,*l* | |
| −7 | −5 | 5 |
| −5 | −6 | 9 |
| −3 | −8 | 8 |
| −1 | −14 | 14 |
| | 5,4,*l* | |
| −4 | −2 | 4 |
| −2 | 3 | 4 |
| 0 | 4 | 5 |
| | 5,5,*l* | |
| −11 | −7 | 4 |
| −9 | −5 | 5 |
| −5 | −19 | 19 |
| −3 | −10 | 11 |
| −1 | −13 | 11 |
| 1 | −15 | 16 |
| 3 | −9 | 11 |
| 5 | −5 | 8 |
| 7 | −7 | 7 |
| | 5,6,*l* | |
| −10 | −12 | 8 |
| −8 | −8 | 7 |
| −6 | −19 | 19 |
| −4 | −32 | 32 |
| −2 | −33 | 27 |
| 0 | −6 | 4 |
| 2 | −34 | 29 |
| 4 | −31 | 32 |
| 6 | −12 | 11 |
| 8 | −12 | 13 |
| 10 | −10 | 7 |
| | 5,7,*l* | |
| −11 | −8 | 4 |
| −9 | −8 | 7 |
| −7 | −6 | 5 |
| −5 | −22 | 23 |
| −3 | −25 | 25 |
| −1 | −13 | 12 |
| 1 | −17 | 19 |
| 3 | −25 | 25 |
| 5 | −14 | 14 |
| 7 | −8 | 10 |
| 9 | −8 | 9 |
| | 5,8,*l* | |
| −6 | 5 | 5 |
| −4 | 6 | 9 |
| −2 | 6 | 8 |
| 0 | 6 | 7 |
| 2 | 10 | 13 |
| 4 | 6 | 8 |
| 8 | 2 | 4 |
| | 5,9,*l* | |
| −11 | 6 | 4 |
| −7 | −3 | 6 |
| −5 | 17 | 17 |
| −3 | 20 | 20 |
| 3 | 16 | 17 |
| 5 | 11 | 10 |
| 9 | 4 | 4 |

| *l* | $F_c$ | $\lvert F_o\rvert$ |
|---|---|---|
| | 5,10,*l* | |
| −8 | −5 | 7 |
| 0 | −14 | 15 |
| 2 | 4 | 6 |
| 4 | 2 | 4 |
| 6 | −7 | 12 |
| 8 | −2 | 3 |
| | 5,11,*l* | |
| −9 | −5 | 4 |
| −7 | −8 | 8 |
| −5 | −5 | 6 |
| −3 | −12 | 13 |
| −1 | −14 | 15 |
| 1 | −10 | 11 |
| 3 | −7 | 9 |
| 5 | −8 | 9 |
| 7 | −6 | 6 |
| | 5,12,*l* | |
| −4 | 3 | 5 |
| | 5,13,*l* | |
| −9 | 8 | 6 |
| −7 | 11 | 9 |
| −5 | 10 | 10 |
| −3 | 15 | 16 |
| −1 | 11 | 10 |
| 1 | 15 | 14 |
| 3 | 18 | 18 |
| 5 | 9 | 9 |
| 7 | 6 | 5 |
| | 5,14,*l* | |
| −8 | 7 | 5 |
| −6 | 9 | 9 |
| −4 | 26 | 26 |
| −2 | 19 | 20 |
| 0 | 12 | 12 |
| 2 | 17 | 19 |
| 4 | 19 | 21 |
| 6 | 13 | 14 |
| 8 | 7 | 6 |
| | 5,15,*l* | |
| −7 | 4 | 3 |
| −5 | 5 | 6 |
| −3 | 8 | 9 |
| −1 | 4 | 5 |
| 1 | 7 | 8 |
| 3 | 9 | 12 |
| 5 | 4 | 5 |
| | 5,17,*l* | |
| −7 | 4 | 3 |
| −5 | 3 | 3 |
| −1 | 7 | 8 |
| 1 | 6 | 6 |
| 5 | 2 | 4 |
| | 5,18,*l* | |
| −6 | 8 | 6 |
| −4 | 4 | 4 |
| −2 | 9 | 10 |
| 0 | 11 | 11 |
| 2 | 7 | 8 |
| 4 | 5 | 7 |
| | 5,19,*l* | |
| −1 | 4 | 4 |
| | 5,20,*l* | |
| −4 | −3 | 2 |
| −2 | −3 | 3 |
| 0 | −4 | 4 |
| 2 | −5 | 5 |
| | 5,21,*l* | |
| −1 | −7 | 4 |
| | 6,0,*l* | |
| −12 | −9 | 4 |
| −10 | −18 | 18 |
| −8 | −18 | 18 |
| −6 | −26 | 28 |
| −4 | −41 | 46 |
| −2 | −32 | 40 |
| 0 | −30 | 32 |
| 2 | −44 | 50 |
| 4 | −32 | 33 |

TABLE 2. (*Continued.*)

| $h$ | $F_c$ | $\lvert F_o\rvert$ | $h$ | $F_c$ | $\lvert F_o\rvert$ | $h$ | $F_c$ | $\lvert F_o\rvert$ | $h$ | $F_c$ | $\lvert F_o\rvert$ | $h$ | $F_c$ | $\lvert F_o\rvert$ | $h$ | $F_c$ | $\lvert F_o\rvert$ |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 6,1,*l* | | | 6,9,*l* | | 2 | −5 | 5 | 4 | 5 | 8 | −5 | 13 | 13 | −1 | −8 | 10 |
| −11 | −9 | 6 | −11 | 3 | 3 | 4 | −3 | 3 | 6 | 2 | 5 | −3 | 14 | 14 | 1 | −6 | 7 |
| −9 | −7 | 6 | −5 | 7 | 7 | | | | | | | −1 | 31 | 33 | | | |
| −5 | −21 | 21 | −3 | 12 | 13 | | 7,1,*l* | | | 7,11,*l* | | 1 | 14 | 14 | | 8,14,*l* | |
| −3 | −27 | 31 | 1 | 3 | 4 | −11 | 6 | 3 | −5 | 7 | 7 | | | | −2 | 5 | 6 |
| −1 | −11 | 11 | 3 | 12 | 13 | −9 | 9 | 9 | −3 | 5 | 6 | | 8,2,*l* | | 0 | 6 | 8 |
| 5 | −20 | 18 | 5 | 3 | 4 | −7 | 10 | 9 | −1 | 8 | 10 | −2 | −1 | 4 | 4 | 4 | 5 |
| | | | 7 | 4 | 5 | −5 | 20 | 20 | 1 | 9 | 9 | | | | | | |
| | 6,2,*l* | | 9 | 3 | 3 | −3 | 10 | 13 | 3 | 5 | 6 | | 8,3,*l* | | | 8,15,*l* | |
| −4 | 4 | 3 | | | | −1 | 26 | 28 | 5 | 8 | 9 | −5 | −7 | 7 | −7 | 6 | 5 |
| −2 | 4 | 10 | | 6,10,*l* | | 1 | 32 | 30 | 7 | 5 | 4 | −1 | −8 | 7 | −5 | 7 | 7 |
| | | | −6 | 4 | 5 | 3 | 12 | 12 | | | | | | | −3 | 6 | 7 |
| | 6,3,*l* | | 0 | 8 | 8 | 5 | 19 | 16 | | 7,12,*l* | | | 8,4,*l* | | −1 | 13 | 15 |
| −7 | −3 | 5 | 2 | 7 | 8 | | | | −6 | −4 | 4 | −4 | 12 | 14 | 1 | 8 | 10 |
| −5 | 2 | 3 | 4 | 3 | 4 | | 7,2,*l* | | −4 | −2 | 3 | −2 | 13 | 12 | | | |
| −1 | −3 | 4 | | | | −10 | 6 | 4 | −2 | −5 | 6 | 0 | 6 | 5 | | 8,16,*l* | |
| 1 | −4 | 5 | | 6,11,*l* | | −6 | 12 | 11 | | | | | | | −6 | 5 | 5 |
| 3 | −9 | 9 | −7 | 8 | 7 | −4 | 10 | 9 | | 7,13,*l* | | | 8,5,*l* | | 0 | 8 | 9 |
| | | | −5 | 11 | 11 | −2 | 25 | 21 | −9 | −7 | 4 | −7 | 8 | 7 | | | |
| | 6,4,*l* | | −3 | 12 | 12 | | | | −7 | −10 | 8 | −5 | 7 | 6 | | 8,18,*l* | |
| −8 | −6 | 5 | −1 | 17 | 18 | | 7,3,*l* | | −5 | −13 | 12 | −3 | 8 | 10 | −4 | 3 | 4 |
| −6 | −8 | 6 | 1 | 12 | 11 | −5 | 5 | 6 | −3 | −6 | 6 | −1 | 8 | 7 | −2 | 3 | 4 |
| −4 | −17 | 18 | 3 | 7 | 6 | −3 | −9 | 11 | −1 | −14 | 14 | 1 | 15 | 13 | 2 | 3 | 4 |
| −2 | −17 | 16 | 5 | 15 | 17 | −1 | 6 | 4 | 1 | −16 | 15 | | | | | | |
| 0 | −13 | 13 | 7 | 7 | 7 | 1 | 11 | 12 | 3 | −9 | 9 | | 8,6,*l* | | | 8,19,*l* | |
| 2 | −15 | 14 | 9 | 4 | 2 | | | | 5 | −10 | 9 | −2 | −5 | 5 | −1 | 6 | 5 |
| 6 | −10 | 11 | | 6,12,*l* | | | 7,4,*l* | | 7 | −6 | 5 | | | | 1 | 7 | 5 |
| 8 | −8 | 7 | −10 | 6 | 3 | −2 | 4 | 5 | | | | | 8,7,*l* | | | | |
| | | | −8 | 9 | 6 | | | | | 7,14,*l* | | −9 | −13 | 9 | | 9,1,*l* | |
| | 6,5,*l* | | −6 | 11 | 9 | | 7,5,*l* | | −8 | −5 | 4 | −7 | −18 | 17 | −7 | −15 | 16 |
| −11 | −5 | 3 | −4 | 9 | 9 | −11 | 4 | 2 | −6 | −11 | 9 | −5 | −14 | 14 | −1 | −20 | 25 |
| −9 | −7 | 5 | −2 | 11 | 9 | −9 | 7 | 5 | −4 | −12 | 11 | −3 | −20 | 21 | 1 | −17 | 18 |
| −7 | −5 | 5 | 0 | 15 | 13 | −7 | 11 | 8 | −2 | −18 | 17 | −1 | −27 | 25 | | | |
| −5 | −9 | 8 | 2 | 13 | 12 | −5 | 5 | 5 | 0 | −16 | 16 | 1 | −25 | 25 | | 9,5,*l* | |
| −3 | −16 | 13 | 4 | 10 | 10 | −3 | 16 | 17 | 2 | −10 | 10 | 3 | −13 | 12 | 1 | −12 | 13 |
| −1 | −7 | 6 | 6 | 7 | 7 | −1 | 10 | 8 | 4 | −12 | 12 | 7 | −14 | 13 | | | |
| 1 | −8 | 8 | 8 | 5 | 4 | 1 | 8 | 4 | 6 | −13 | 12 | | | | | 9,7,*l* | |
| 3 | −15 | 15 | | | | 3 | 15 | 13 | | | | | 8,8,*l* | | | | |
| 7 | −8 | 9 | | 6,13,*l* | | | | | | 7,15,*l* | | −10 | −8 | 5 | 1 | −18 | 20 |
| 9 | −5 | 5 | −5 | 5 | 7 | | 7,6,*l* | | −5 | −5 | 4 | −8 | −14 | 11 | | | |
| | | | −3 | 7 | 7 | −10 | 11 | 6 | −1 | −5 | 5 | −6 | −11 | 12 | | 10,0,*l* | |
| | 6,6,*l* | | −1 | 4 | 8 | −8 | 13 | 12 | 1 | −8 | 8 | −4 | −13 | 16 | −8 | −23 | 22 |
| −6 | 3 | 4 | 5 | 6 | 7 | −6 | 11 | 9 | 3 | −4 | 4 | −2 | −21 | 22 | −6 | −24 | 25 |
| −4 | 3 | 4 | 7 | 3 | 4 | −4 | 26 | 24 | 5 | −4 | 4 | 0 | −24 | 23 | −4 | −20 | 23 |
| −2 | 2 | 4 | | | | −2 | 20 | 18 | | | | 2 | −15 | 16 | −2 | −27 | 27 |
| 0 | 3 | 8 | | 6,14,*l* | | 0 | 23 | 19 | | 7,17,*l* | | 4 | −8 | 7 | 0 | −35 | 33 |
| 2 | 6 | 6 | −6 | −5 | 5 | | | | −3 | −5 | 5 | 6 | −14 | 14 | 2 | −30 | 29 |
| 4 | 4 | 4 | −4 | −6 | 7 | | 7,7,*l* | | 3 | −5 | 5 | | | | 4 | −19 | 17 |
| | | | −2 | −7 | 8 | −11 | 6 | 3 | | | | | 8,9,*l* | | 6 | −16 | 12 |
| | 6,7,*l* | | 0 | −8 | 8 | −9 | 8 | 6 | | 7,18,*l* | | −3 | −4 | 7 | | 10,1,*l* | |
| −11 | 10 | 6 | 2 | −8 | 9 | −7 | 10 | 9 | −4 | −8 | 7 | −1 | −7 | 10 | | | |
| −9 | 12 | 10 | 4 | −7 | 8 | −5 | 11 | 10 | −2 | −7 | 6 | 1 | −5 | 7 | −3 | −17 | 17 |
| −7 | 12 | 9 | 6 | −4 | 5 | −3 | 19 | 22 | 0 | −6 | 6 | | | | −1 | −22 | 21 |
| −5 | 24 | 22 | | | | −1 | 15 | 18 | 2 | −8 | 8 | | 8,11,*l* | | 1 | −14 | 13 |
| −3 | 33 | 35 | | 6,15,*l* | | 1 | 16 | 18 | 4 | −6 | 6 | −5 | −8 | 12 | | | |
| −1 | 19 | 17 | −5 | −10 | 9 | 3 | 16 | 18 | | | | −3 | −11 | 11 | | 10,7,*l* | |
| 1 | 22 | 27 | −3 | −12 | 12 | | | | | 7,19,*l* | | −1 | −11 | 12 | 1 | 18 | 16 |
| 3 | 33 | 35 | −1 | −8 | 8 | | 7,8,*l* | | −3 | −3 | 3 | 1 | −5 | 7 | | | |
| 5 | 13 | 12 | 1 | −7 | 7 | −4 | −3 | 6 | | | | 3 | −9 | 10 | | 12,0,*l* | |
| 7 | 14 | 15 | 3 | −7 | 9 | −2 | −3 | 5 | | 8,0,*l* | | 5 | −9 | 9 | −8 | 12 | 10 |
| 9 | 10 | 11 | 5 | −10 | 10 | 0 | −6 | 6 | −10 | 13 | 11 | | | | −6 | 17 | 18 |
| | | | 7 | −5 | 5 | 2 | −7 | 8 | −8 | 24 | 23 | | 8,12,*l* | | −4 | 20 | 19 |
| | 6,8,*l* | | | | | | | | −6 | 36 | 37 | −8 | −8 | 6 | −2 | 18 | 18 |
| −10 | 11 | 7 | | 6,16,*l* | | | 7,9,*l* | | −4 | 18 | 19 | −6 | −13 | 15 | 0 | 15 | 16 |
| −8 | 8 | 7 | −4 | −4 | 4 | −3 | −14 | 15 | −2 | 31 | 36 | −4 | −8 | 8 | 2 | 24 | 19 |
| −6 | 12 | 11 | 2 | −3 | 5 | −1 | −8 | 8 | 0 | 56 | 57 | −2 | −9 | 8 | 4 | 20 | 15 |
| −4 | 30 | 26 | | | | 1 | −5 | 5 | 2 | 27 | 28 | 0 | −15 | 16 | | | |
| −2 | 21 | 21 | | 6,17,*l* | | 3 | −8 | 9 | 4 | 17 | 16 | 2 | −12 | 11 | | 14,0,*l* | |
| 0 | 11 | 10 | −1 | 3 | 4 | 7 | −9 | 11 | 6 | 22 | 20 | 4 | −9 | 9 | −6 | −12 | 12 |
| 2 | 24 | 22 | 3 | 2 | 3 | | | | | | | | | | −4 | −15 | 17 |
| 4 | 18 | 19 | | | | | 7,10,*l* | | | 8,1,*l* | | | 8,13,*l* | | 2 | −13 | 11 |
| 6 | 11 | 11 | | 6,18,*l* | | −6 | 5 | 8 | −9 | 9 | 6 | −5 | −8 | 9 | 4 | −14 | 10 |
| 8 | 11 | 13 | 0 | −4 | 5 | −2 | 6 | 7 | −7 | 12 | 11 | −3 | −6 | 7 | | | |
| 10 | 7 | 4 | | | | | | | | | | | | | | | |

and one of the carbon atoms of each of the pyridine nuclei must occupy special positions on the two-fold axes. The asymmetric unit would then consist of two copper atoms, two acetate groups, and the nitrogen and three carbon atoms of each of the pyridine molecules.

By using the phases of those structure factors to which the copper atoms had a reasonable contribution, together with the corresponding observed structure amplitudes, a three-dimensional Fourier synthesis was computed. This electron-density distribution confirmed the binuclear structure and led to co-ordinates for the light atoms (excluding hydrogen atoms). The atomic positions were refined by successive three-dimensional Fourier syntheses.

The maxima in the electron-density distribution were determined by fitting a ten-parameter

Gaussian function to 27 values for the electron density about the maximum value.[6] The co-ordinates were corrected for termination-of-series errors by the back-shift method.[7] Scattering-factor curves of Berghuis *et al.*[8] were used for all atoms; the values for copper were corrected for dispersion from the values given by Dauben and Templeton.[9] A temperature factor, $\exp -(B \sin^2\theta/\lambda^2)$, with $B = 2{\cdot}1$ Å$^2$ for the copper atoms and $B = 3{\cdot}6$ Å$^2$ for the other atoms, was applied. The standard deviations of the atomic co-ordinates were estimated by Cruickshank's method.[10] The final atomic co-ordinates, together with their root-mean-square, estimated standard deviations are listed in Table 1. The calculated structure factors and the observed structure amplitudes are given in Table 2. The final discrepancy factor ($R$), based on the 1200 observed reflections, was 0·13.

## Discussion

The binuclear molecules are arranged along the two-fold axes as shown in Fig. 1. The intermolecular distances (see Fig. 1) indicate that the crystal is truly " molecular " with only van der Waals's forces acting between molecules. These forces operate between the pyridine nuclei of one molecule and methyl groups and pyridine rings of other molecules which lie along neighbouring two-fold axes; there is no contact between molecules on the same two-fold axis (distance of separation 4·82 Å).

Table 3.

Bond distances and angles.

| Bond | Length (Å) | σ (Å) | Bond | Length (Å) | σ (Å) | Bond | Length (Å) | σ (Å) |
|---|---|---|---|---|---|---|---|---|
| Cu(1)–O(3) ..... | 1·985 | 0·010 | C(1)–O(1) ..... | 1·247 | 0·016 | C(8)–N(1) ..... | 1·379 | 0·014 |
| Cu(1)–O(4) ..... | 1·973 | 0·010 | C(1)–O(4) ..... | 1·247 | 0·015 | C(3)–N(2) ..... | 1·377 | 0·016 |
| Cu(2)–O(2) ..... | 1·985 | 0·010 | C(2)–O(2) ..... | 1·231 | 0·021 | | | |
| Cu(2)–O(1) ..... | 1·982 | 0·011 | C(2)–O(3) ..... | 1·231 | 0·021 | C(3)–C(4) ..... | 1·381 | 0·018 |
| | | | | | | C(7)–C(8) ..... | 1·411 | 0·019 |
| Cu(1)–N(1) ..... | 2·122 | 0·009 | C(1)–C(6) ..... | 1·467 | 0·022 | C(7)–C(9) ..... | 1·433 | 0·021 |
| Cu(2)–N(2) ..... | 2·129 | 0·011 | C(2)–C(5) ..... | 1·540 | 0·026 | C(4)–C(10) ..... | 1·412 | 0·018 |
| Cu(1)–Cu(2) ... | 2·630 | 0·003 | | | | | | |

| Angle | Value | σ | Angle | Value | σ | Angle | Value | σ |
|---|---|---|---|---|---|---|---|---|
| O(3)–Cu(1)–O(4) | 89·0° | 0·5° | O(3)–C(2)–O(2)... | 127·3° | 0·9° | C(8)–N(1)–C(8′) | 117·9° | 1·5° |
| O(1)–Cu(2)–O(2) | 88·2 | 0·5 | O(4)–C(1)–O(1)... | 122·9 | 0·9 | C(3)–N(2)–C(3′) | 116·4 | 1·5 |
| | | | | | | N(1)–C(8)–C(7)... | 125·2 | 0·9 |
| Cu(1)–O(3)–C(2) | 122·6 | 0·7 | O(3)–C(2)–C(5)... | 115·0 | 0·9 | N(2)–C(3)–C(4)... | 121·5 | 0·9 |
| Cu(1)–O(4)–C(1) | 123·6 | 0·7 | O(1)–C(1)–C(6)... | 118·1 | 0·9 | C(8)–C(7)–C(9)... | 113·7 | 0·9 |
| Cu(2)–O(2)–C(2) | 122·6 | 0·7 | | | | C(3)–C(4)–C(10) | 120·5 | 0·9 |
| Cu(2)–O(1)–C(1) | 125·0 | 0·7 | | | | C(7)–C(9)–C(7′) | 124·2 | 1·5 |
| | | | | | | C(4)–C(10)–C(4′) | 116·5 | 1·5 |

The bond distances and bond angles in the molecule are listed in Table 3 and shown diagrammatically in Fig. 2. The variation in bond length for chemically similar bonds is well within experimental error; the apparently large difference between the two C–$CH_3$ bond lengths is only twice the estimated standard deviation of their difference. The copper–copper distance (2·63 Å) is the same as that found in copper acetate monohydrate [1] (2·64 Å), and the other bond lengths agree with the values reported for other compounds.[11] There is no significant difference between the carbon–nitrogen and carbon–carbon bond lengths in the pyridine molecules; the bond angles vary from 114° to 125° but the mean value is 119·5°. Since the values found for the same angle in the two pyridine molecules are not consistent, the variations are probably due to experimental error.

[6] Shoemaker, Donohue, Shomaker, and Corey, *J. Amer. Chem. Soc.*, 1950, **72**, 2328.
[7] Booth, *Proc. Roy. Soc.*, 1946, *A*, **188**, 77.
[8] Berghuis, Haanapel, Potters, Loopstra, MacGillavry, and Veenendaal, *Acta Cryst.*, 1955, **8**, 478.
[9] Dauben and Templeton, *Acta Cryst.*, 1955, **8**, 841.
[10] Cruickshank, *Acta Cryst.*, 1948, **2**, 65; Cruickshank and Rollett, *ibid.*, 1953, **6**, 705.
[11] " Tables of Interatomic Distances and Configuration in Molecules and Ions," *Chem. Soc. Special Publ.* No. 11; see also Barclay and Kennard, *J.*, 1961, 3289.

Each copper atom is joined by covalent bonds (1·98 Å in length) to four oxygen atoms lying in a plane which is approximately normal to the two-fold axis. The copper atoms are 0·22 Å out of these planes towards the nitrogen atoms of the pyridine rings. The copper–nitrogen bond is slightly longer (2·13 Å) than expected for a covalent bond (1·95—2·04 Å) but is shorter than usually found for the fifth and sixth bonds to copper atoms (2·6—2·8 Å for Cu–N and 2·2—3·0 Å for Cu–O bonds).[11] The four oxygen atoms and the nitrogen atom form a slightly distorted tetragonal-pyramidal co-ordination about the copper atom. The sixth, " octahedral," site is occupied by a second copper atom at 2·63 Å.

The two pyridine nuclei are planar, but the angle between the planes of the two pyridine

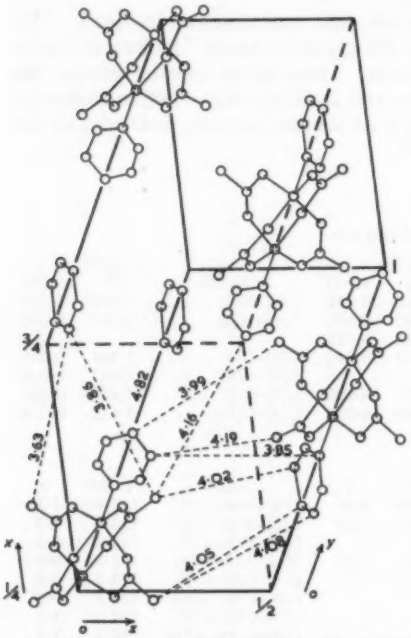


FIG. 1. Arrangement of the molecules in the unit cell of monopyridinecopper(II) acetate.

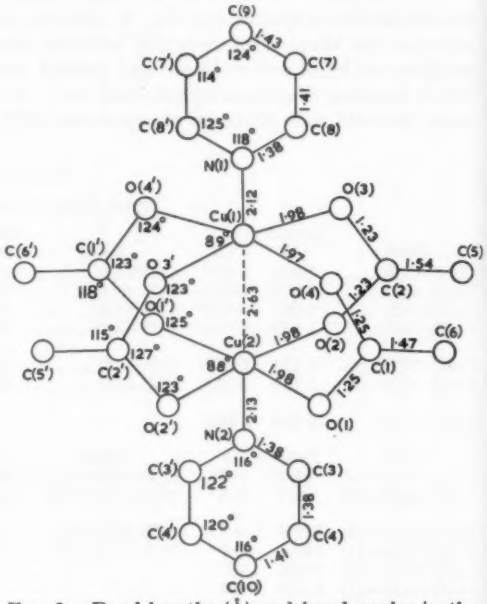


FIG. 2. Bond lengths (Å) and bond angles in the binuclear molecules.

rings in the one binuclear molecule is 60°. The equations for these planes (calculated by the method of least squares) and the deviations of the atoms from these planes are:

$$0{\cdot}149x - 0{\cdot}004y + 0{\cdot}988z - 0{\cdot}477 = 0$$

[C(9), 0·005; C(7), 0·010; C(8), 0·012; N(1), 0·007 Å]

$$0{\cdot}924x - 0{\cdot}003y + 0{\cdot}383z - 2{\cdot}872 = 0$$

[C(10), 0·004; C(4), 0·008; C(3), 0·008; N(2), 0·004 Å]

The close approach of the two copper atoms in the binuclear unit indicates the presence of a δ-bond between them. The low magnetic moment at room temperature (μ 1·40 B.M.) of monopyridinecopper(II) acetate [12] is the same as that of copper acetate monohydrate and may be explained in the same way as due to an interaction between the copper atoms in the binuclear molecule.[2]

[12] Waterman, personal communication.

[*Note added October 17th*, 1961]. Hanic, Stempelova, and Hanicova (*Chem. Zvesti*, 1961, **15**, 102) have reported the structure of an orthorhombic form of monopyridine-copper(II) acetate. This crystal is built up of binuclear molecules similar to those reported here except that the two pyridine molecules of the binuclear unit lie in the same plane.

The authors thank Mr. J. C. Taylor for powder photographs.

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## 1038. *Experiments Confirming the Structure of Shellolic Acid.*

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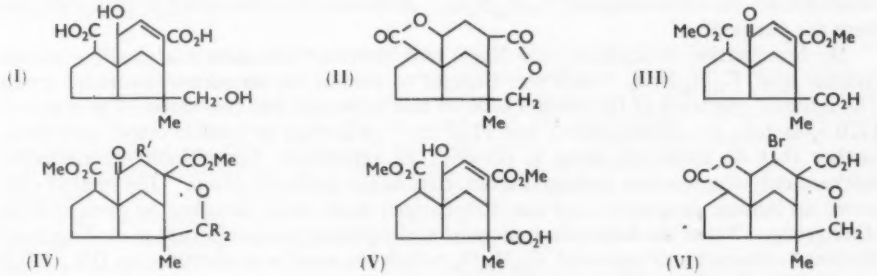
Experiments with shellolic acid support its formulation (I) proposed recently by Yates and Field.

IN view of the report by Yates and Field [1] on the sesquiterpene shellolic acid, to which they assign the structure (I), we record some results of ours which confirm their findings.

For the isolation of the acid we employed Gidvani's method [2] but in our hands yields were variable and were considerably below those claimed.[2-4] The crude hydrolysis product of shellac contains a number of other acids closely related to shellolic acid,[4] and from mother liquors of dimethyl shellolate we obtained small amounts of an isomeric αβ-unsaturated ester.




In agreement with the proposed structure, dimethyl shellolate did not form an isopropylidene derivative, and Kuhn–Roth oxidation of the ester and of dihydroshellolic acid (below) showed the presence of one *C*-methyl group. With toluene-*p*-sulphonyl chloride in pyridine dimethyl shellolate gave only a monotoluene-*p*-sulphonate. The ultraviolet and infrared spectra of the acid and of dimethyl shellolate were consistent with the conjugated position of the double bond. In addition, three bands in the C–H deformation region ($\nu_{max.}$ in Nujol 772, 783, and 788 cm.$^{-1}$), absent in the spectrum of the dihydrocompound, strongly suggested the presence of a vinylic hydrogen atom for which the American workers obtained evidence by nuclear magnetic resonance. The double bond was rather unreactive and dimethyl shellolate did not react with perphthalic acid, but hydrogenation in presence of platinum oxide and treatment of the resulting oil with sodium hydrogen carbonate afforded the crystalline dilactone (II) obtained by Yates and Field [1]

[1] Yates and Field, *J. Amer. Chem. Soc.*, 1960, **82**, 5764.
[2] Gidvani, *J.*, 1944, 306.
[3] Harries and Nagel, *Ber.*, 1922, **55**, 3833.
[4] Kirk, Spoerri, and Gardner, *J. Amer. Chem. Soc.*, 1941, **63**, 1243.

by a similar method. The same product was obtained directly by hydrogenation of shellolic acid. Oxidation of the dilactone with alkaline permanganate gave, in small yield, a crystalline dicarboxylic acid lactone, $C_{15}H_{18}O_6$, formed, presumably, by opening of the lactone ring and oxidation of the primary alcohol group.

By oxidation of dimethyl shellolate with six equivalents of chromic acid we obtained results essentially similar to those of Yates and Field.[1] The principal product was the oxo-acid formulated by them as (III); in some experiments the isomeric oxo-lactone (IV; $R_2 = O$, $R' = H$), which they describe, was also obtained. Both products were converted by methanol and sulphuric acid into the trimethyl ester, prepared also from the acid with methyl iodide and potassium carbonate. Reduction of the trimethyl ester with sodium borohydride led to a mixture from which the (oily) alcohol was isolated by chromatography. Catalytic reduction of the acid (III) with palladium in ethanol afforded an alcohol (V) by preferential reduction of the carbonyl group ($\lambda_{max.}$ 225 mμ, log ε 3·74; $\nu_{max.}$ in Nujol 3500, 1730, 1710, 1680sh cm.$^{-1}$).

With manganese dioxide,[5] dimethyl shellolate was converted in small yield into the dehydro-compound (IV; $R = R' = H$) obtained by Yates and Field.[1] In our hands, however, the main product was the acid (V) formed surprisingly by preferential oxidation of the non-conjugated, but more exposed, primary alcohol group. The product was identical with the acid obtained, as above, by catalytic reduction of the acid (III), and on oxidation with chromic acid afforded the oxo-lactone (IV; $R_2 = O$, $R' = H$) mentioned above.

Oxidation of dimethyl shellolate with hydrogen peroxide and osmium tetroxide afforded a crystalline lactone, $C_{16}H_{22}O_7$ ($\nu_{max.}$ in Nujol 1720 cm.$^{-1}$) by hydroxylation of the double bond and δ-lactonisation with loss of the elements of methanol. Again, treatment of the dihydroxy-dilactone, $C_{15}H_{18}O_6$, obtained by Nagel and Mertens [6] from shellolic acid and alkaline permanganate, with lead tetra-acetate gave an oily dicarbonyl compound, isolated as its bis-semicarbazone, $C_{17}H_{24}N_6O_7$. Both reactions proceeded in poor yield and were not pursued.

By bromination of shellolic acid Nagel and Mertens [6] obtained a crystalline bromo-lactonic acid, $C_{15}H_{17}BrO_5$, which was thought to contain an unreactive hydroxyl group. The infrared spectrum of the methyl ester of this substance has two carbonyl maxima, at 1770 (γ-lactone or α-bromo-ester) and 1720 cm.$^{-1}$ (δ-lactone or normal ester), and shows further that no hydroxyl group is present; in agreement, Zerewitinoff determination discloses only one reactive hydrogen atom, that in the carboxyl group. The methyl ester shows no ketonic properties, and the fifth oxygen atom must therefore be present in an ether group. From the bromo-lactonic acid and aqueous potassium carbonate Nagel and Mertens [6] obtained a dibasic acid, $C_{15}H_{18}O_6$, which has now been identified as (IV; $CO_2H$ for $CO_2Me$; $R = R' = H$) by the fact that the dimethyl ester was identical with the neutral product (IV; $R = R' = H$) obtained by oxidation of dimethyl shellolate with manganese dioxide. On the basis of these facts the bromo-lactonic acid is represented by the structure (VI) with the bromine atom and the oxygen of the lactone ring in the *cis*-configuration, and its mode of formation recalls that of bromopicrotoxinin from picrotoxinin.[7] The ketone (IV; $R = R' = H$) is also produced by reaction of *N*-bromosuccinimide with dimethyl shellolate in presence of pyridine. A minor product of this reaction, $C_{17}H_{21}BrO_6$, was obtained also by Dr. R. A. W. Johnstone as the main product from reaction in absence of pyridine and is regarded as the α-bromo-ketone (IV; $R = H$, $R' = Br$) (cf. ref. 8). Its ultraviolet absorption ($\lambda_{max.}$ 278 mμ; log ε 1·93) indicates that the bromine is equatorial.[9] The infrared spectrum shows only one carbonyl maximum, at

[5] Attenburrow *et al.*, *J.*, 1952, 1094; Evans, *Quart. Rev.*, 1959, **13**, 61.
[6] Nagel and Mertens, *Ber.*, 1939, **72**, 985.
[7] Conroy, *J. Amer. Chem. Soc.*, 1952, **74**, 491; 1957, **79**, 1726.
[8] Stuckwisch, Hammer, and Blau, *J. Org. Chem.*, 1957, **22**, 1678.
[9] Cookson, *J.*, 1954, 282.

1745 cm.$^{-1}$ (normal ester and α-bromo-ketone in a six-membered ring); there is no absorption indicating olefinic unsaturation and no hydroxyl band.

## Experimental

*Isolation of Shellolic Acid.*—In the present work best results were obtained by using Super-Blonde Shellac. Shellolic acid was isolated as its zinc salt as described by Gidvani.[2] Yields from 500 g. of shellac varied from 37—78 g. depending on the shellac used.

For the isolation of dimethyl shellolate the dried and powdered zinc salts (70 g.) were esterified directly with methanol (1 l.) containing hydrogen chloride (3%) at room temperature for 4—5 days. The solution was partly neutralised with solid sodium hydrogen carbonate, and methanol removed under reduced pressure with slight warming. Water was added and the product was extracted with ether and washed with sodium hydrogen carbonate and with water. A reddish-brown viscous oil was obtained from which dimethyl shellolate was precipitated as an amorphous powder (11 g.), m. p. 142—150°, by trituration with ether. It crystallised from ethyl acetate as colourless prisms, m. p. 151—152·5° (Found: C, 63·1; H, 7·6. Calc. for $C_{17}H_{24}O_6$: C, 63·0; H, 7·5%), $[\alpha]_{5461}^{18\cdot1}$ +47·6°, +47·2°, $\lambda_{max.}$ (in EtOH) 229 mμ (log ε 3·77), $\nu_{max.}$ (in $CHCl_3$) 3350, 1720, 1705, 1658 cm.$^{-1}$.

The quantities of dimethyl shellolate isolated varied greatly in different experiments. The zinc salt should be esterified as soon as possible after isolation as changes occur on storage which lower the yield of ester.

In other experiments with different types of lac, very much smaller yields of dimethyl shellolate were obtained as shown in the Table. Usually about 25% of the oil resulting from esterification of the zinc salts was isolated as dimethyl shellolate. The remainder, consisting probably of a mixture of esters of several hydroxy-acids similar to shellolic acid (cf. Kirk, Spoerri, and Gardner [4]), remained for the most part uncrystallisable. On some occasions further crystalline material separated on prolonged storage. Fractional crystallisation of this afforded dimethyl shellolate and a small amount of another product, m. p. 152·5—153·5°, depressed to 126—131° when mixed with dimethyl shellolate (Found: C, 62·2, 62·8; H, 7·9, 6·9. Calc. for $C_{17}H_{24}O_6$: C, 63·0; H, 7·5%), $[\alpha]_{5461}^{20\cdot2}$ +58·6° (in EtOH), $\lambda_{max.}$ (in EtOH) 229 mμ (log ε 3·77). Hydrolysis of this ester afforded an acid, which softened at 208° and melted at 220° (decomp.).

| Type of lac | Total quantity of lac (kg.) | Quantity of dimethyl shellolate obtained (g.) | (%) |
|---|---|---|---|
| Kusum (scraped) | 18 | 20·1 | 0·112 |
| Siam | 2·5 | 1·4 | 0·056 |
| Calcutta (dewaxed) | 3·5 | 6·9 | 0·197 |
| Ber | 4·0 | 0·5 | 0·012 |
| Palas | 4·0 | 1·0 | 0·025 |
| Kusmi | 2·5 | 0·3 | 0·012 |
| Angela deora shellac | 23 | 182·6 | 0·794 |

Hydrolysis of the remaining syrupy material with sodium hydroxide afforded a gum.

Treatment of dimethyl shellolate (1 equiv.) with toluene-*p*-sulphonyl chloride (2 equiv.) in boiling pyridine for 2 hr. afforded, after chromatography, a *monotoluene*-p-*sulphonate*, m. p. 84—85° (from benzene–light petroleum), $[\alpha]_{5461}^{21}$ (*c* 2·351 in EtOH) +4·30° (Found: C, 59·8; H, 6·3; S, 6·85. $C_{24}H_{30}O_8S$ requires C, 60·2; H, 6·3; S, 6·7%).

Hydrolysis of dimethyl shellolate with sodium hydroxide as described by Kirk, Spoerri, and Gardner [4] afforded shellolic acid, m. p. 199—201° (decomp.) (from water), $\lambda_{max.}$ (in EtOH) 228 mμ (log ε 3·73), $[\alpha]_{5461}^{17\cdot6}$ +26·3°. Potentiometric titration of the acid with sodium hydroxide gave dissociation constants $pK_1$ 4·00 and $pK_2$ 5·08 (kindly determined for us by Dr. J. C. Speakman). The *di*-p-*bromophenacyl ester* (from methanol) had m. p. 141—142° (Found: C, 54·0; H, 4·45. $C_{31}H_{30}Br_2O_8$ requires C, 53·9; H, 4·35%).

*Hydrogenation of Dimethyl Shellolate.*—Microhydrogenation with platinum oxide in ethanol caused uptake of 0·88$H_2$. On a larger scale dimethyl shellolate (1 g.) in ethanol (10 c.c.) was hydrogenated with platinum oxide (50 mg.) (8 hr.); the viscous oil obtained was treated overnight at room temperature with potassium hydrogen carbonate (2·5 g.) in methanol (125 c.c.) and water (50 c.c.); methanol was removed under reduced pressure, the dihydro-dilactone being obtained on acidification. It crystallised from water or from aqueous ethanol as needles, m. p.



XUM

150—151° [Found: C, 68·4; H, 6·8%; equiv. (by titration), 119, 121. Calc. for $C_{15}H_{18}O_4$: C, 68·7; H, 6·9%; equiv., 131]. There was no high-intensity ultraviolet absorption above 215 mμ; $\nu_{max.}$ were at 1765 and 1740 cm.$^{-1}$ in $CHCl_3$.

The dihydro-dilactone was also obtained when shellolic acid (5 g.) was reduced with 2% palladised strontium carbonate (7 g.) in ethanol (300 c.c.) at 50°/120 atm.

The dihydro-dilactone (0·52 g.) was oxidised with potassium permanganate (0·42 g.) and potassium hydroxide (0·67 g.) in water (25 c.c.). Next morning manganese dioxide was filtered off and washed with boiling water, and the combined filtrates were evaporated to small volume and made acid to Congo Red. The precipitate was collected and crystallised from water, affording the *dicarboxylic acid lactone* as blades, m. p. 223—226° (Found: C, 61·4; H, 6·4. $C_{15}H_{18}O_6$ requires C, 61·2; H, 6·1%). Direct titration with barium hydroxide gave an equivalent weight of 157, but addition of an excess, warming, cooling, and back-titration gave a value of 92·7.

*Oxidation of Dimethyl Shellolate with Chromic Acid.*—Chromium trioxide in sulphuric acid [10] (2·45 c.c.) was added dropwise to a solution of the ester (1 g.) in acetone (100 c.c.) at 5°. When reaction was complete the solution was diluted with water and extracted with ether, and the extract was treated with aqueous sodium carbonate. The product (820 mg.) obtained from the alkaline solution crystallised from ether–methyl acetate and afforded the keto-acid (III) as prisms, m. p. 139—140° (Found: C, 60·8; H, 6·0. Calc. for $C_{17}H_{20}O_7$: C, 60·7; H, 6·0%), $\lambda_{max.}$ (in EtOH) 240, 343—353 mμ (log ε 3·97, 1·80). The *oxime* formed needles (from aqueous methanol), m. p. 161—162° (Found: N, 3·9. $C_{17}H_{21}NO_7$ requires N, 4·1%). Treatment of the keto-acid (100 mg.) with piperonaldehyde (50 mg.) in methanol (1 c.c.) containing 10N-sodium hydroxide (3 drops) afforded a *substance*, m. p. 233—236° (from ether), which appears to have resulted from hydrolysis of one of the ester groups (Found: C, 59·8; H, 5·75. $C_{16}H_{18}O_7$ requires C, 59·6; H, 5·6%). The trimethyl ester, prepared from the keto-acid with methyl iodide and potassium carbonate in acetone, formed needles, m. p. 94° (from ether) (Found: C, 61·6; H, 6·0. Calc. for $C_{18}H_{22}O_7$: C, 61·7; H, 6·3%), $\nu_{max.}$ (in $CCl_4$) 1740, 1696 cm.$^{-1}$, $\lambda_{max.}$ (in EtOH) 239, 345—355 mμ (log ε 3·97, 1·77).

In some experiments a mixture was obtained from which the keto-lactone (IV: $R_2$ = O, R′ = H) was isolated by crystallisation from ether as prisms, m. p. 144—146°, depressed when mixed with the keto-acid (Found: C, 60·5; H, 5·0. Calc. for $C_{17}H_{20}O_7$: C, 60·7; H, 6·0%), $\lambda_{max.}$ (in EtOH) 280 mμ (log ε 1·72), $\nu_{max.}$ (in Nujol) 1790, 1760, 1720 cm.$^{-1}$.

Esterification of either product (100 mg.) with methanol (10 c.c.) and sulphuric acid (1 c.c.) afforded an ester, m. p. 94—95°, not depressed when mixed with the trimethyl ester prepared from the acid as described above; the infrared spectra were identical.

Hydrogenation of the keto-acid with palladium–charcoal in ethanol afforded the *dihydro-compound* in quantitative yield as needles, m. p. 195—196° (from ether–methyl acetate) (Found: C, 60·4; H, 6·6. $C_{17}H_{22}O_7$ requires C, 60·3; H, 6·6%).

Reduction of the trimethyl ester (200 mg.) with sodium borohydride (250 mg.) in ethylene glycol dimethyl ether (10 c.c.) afforded a gum (120 mg.) which was chromatographed on silica gel. Benzene–ether (1 : 1) eluted fractions with only weak absorption at 3500 cm.$^{-1}$ and a pronounced band at 1780 cm.$^{-1}$ indicative of a γ-lactone. The *dihydro-compound* was eluted with ether and distilled at 180—190°/0·5 mm. (Found: C, 62·0; H, 7·4. $C_{18}H_{24}O_7$ requires C, 61·4; H, 6·9%), having $\lambda_{max.}$ (in EtOH) 225 mμ (log ε 3·58), $\nu_{max.}$ (in $CCl_4$) 3550, 1727 cm.$^{-1}$.

*Oxidation of Dimethyl Shellolate with Manganese Dioxide.*—The ester was recovered after treatment with manganese dioxide in chloroform solution at room temperature for 16 hr.

In another experiment a stirred solution of dimethyl shellolate (1 g.) in benzene (50 c.c.) was heated on the water bath with manganese dioxide [11] (8 g.) for 16 hr. Manganese dioxide was filtered off and washed with chloroform and with methanol. The recovered gum (900 mg.) partly crystallised when triturated with carbon tetrachloride. Crystallisation from benzene–methanol afforded needles, m. p. 197—199° alone or mixed with the reduction product prepared from the keto-acid as described above (Found: C, 61·0; H, 6·3. $C_{17}H_{22}O_7$ requires C, 60·3; H, 6·6%), $\lambda_{max.}$ (in EtOH) 225—226 mμ (log ε 3·71); the infrared spectra of the two products were identical. The *methyl ester*, prepared with methyl iodide and potassium carbonate, formed prisms, m. p. 109—111° (from ether) (Found: C, 61·0; H, 6·7. $C_{18}H_{24}O_7$ requires C, 61·35; H, 6·9%), $\lambda_{max.}$ (in EtOH) 226 mμ (log ε 3·76), $\nu_{max.}$ (in Nujol), 3550, 1724, 1708 cm.$^{-1}$. Oxidation

[10] Bowers, Halsall, Jones, and Lemin, *J.*, 1953, 2555.
[11] Mancera, Rosenkranz, and Sondheimer, *J.*, 1953, 2189.

of the acid with two equivalents of chromic acid as described above for dimethyl shellolate gave the keto-lactone, m. p. 142—146°, not depressed when mixed with a specimen obtained by oxidation of dimethyl shellolate. The infrared spectra were identical.

The remaining material from the manganese dioxide oxidation was extracted with sodium carbonate, yielding a further 85 mg. of acid. The neutral fraction was chromatographed on silica gel. Benzene–ether (4 : 1) eluted a gum (98 mg.) which partly crystallised when triturated with ether and therefrom afforded the oxo-ether (IV: R = R′ = H) as prisms, m. p. 120—122° (Found: C, 63·4; H, 6·7. Calc. for $C_{17}H_{22}O_6$: C, 63·3; H, 6·9%), $\nu_{max.}$ (in $CHCl_3$) 1725, 1741sh cm.$^{-1}$, no high-intensity absorption above 215 mμ. Elution with ether afforded dimethyl shellolate (145 mg.).

*Oxidation of Dimethyl Shellolate with Osmium Tetroxide and Hydrogen Peroxide.*—To a solution prepared from dimethyl shellolate (0·68 g.) and hydrogen peroxide (0·08 g.) in t-butyl alcohol (38 c.c.) was added at 0° a 0·5% solution of osmium tetroxide in t-butyl alcohol (5 drops). After 5 days at 25° the yellow solution was evaporated to dryness, benzene (75 c.c.) was added, and the mixture warmed and filtered. The residue (0·1 g.) crystallised from Cellosolve as prisms of the *product* which softened at 210° with evolution of gas and finally melted at 232—238° (Found: C, 58·9; H, 6·9; OMe, 10·3. $C_{16}H_{22}O_7$ requires C, 58·9; H, 6·75; OMe, 9·5%), $\nu_{max.}$ (KBr disc) 3300—3500, 1730 cm.$^{-1}$, no high-intensity absorption above 210 mμ.

*Oxidation of Shellolic Acid with Potassium Permanganate.*—The oxidation was carried out as described by Nagel and Mertens.[6] The product softened at 110° and melted at 123—124° (lit., swells at 124°, melts at 162°). This product (0·1 g.) was treated in water with lead tetra-acetate (0·14 g.) in acetic acid (7 c.c.). Next morning 0·1N-sulphuric acid (6·5 c.c.) was added, lead sulphate filtered off, and the solution evaporated to dryness. The sticky residue solidified when triturated with water, but the solid did not crystallise. It was converted into its *semicarbazone*, which prisms (from water), m. p. 270—272° (decomp.).

A slightly purer semicarbazone, m. p. 274—275° (decomp.), was obtained when the permanganate oxidation product (0·615 g.) was oxidised with sodium metaperiodate (0·528 g.) in water (16 c.c.) for 5 days (Found: C, 48·1; H, 5·6; N, 19·7. $C_{17}H_{24}N_6O_7$ requires C, 48·1; H, 5·7; N, 19·8%).

*Bromination of Shellolic Acid.*—The reaction was carried out as described by Nagel and Mertens.[6] The product formed colourless needles (from aqueous methanol), m. p. 235—237° (lit., 226°), after drying for 6 hr. at 110°/0·4 mm. (Found: C, 50·9; H, 4·7; active H, 0·28. Calc. for $C_{15}H_{17}BrO_5$: C, 50·4; H, 4·8; 1 active H, 0·25%), $[\alpha]_D^{18}$ −103·5°. The *methyl ester*, prepared with diazomethane, formed prisms m. p. 174—175° (from cyclohexane) (Found: C, 52·0; H, 5·1; OMe, 8·1. $C_{16}H_{19}BrO_5$ requires C, 51·8; H, 5·2; 10Me, 8·4%).

Reduction of this product (150 mg.) with zinc (0·5 g.) and N-hydrochloric acid (6 c.c.) as described by Nagel and Mertens afforded deoxyshellolic acid as prisms, m. p. 181—184° (from water) (Found: C, 64·9; H, 6·4. Calc. for $C_{15}H_{18}O_5$: C, 64·7; H, 6·5%), log ε 600 at 220 mμ, 980 at 215 mμ. Treatment of the bromo-lactonic acid (215 mg.) with potassium carbonate (150 mg.) in water (0·6 c.c.) on the water bath for 1½ hr. and acidification to Congo Red afforded the dicarboxylic acid (described by Nagel and Mertens [6]) as prisms, m. p. 231—236° (from water) (Found: C, 61·4; H, 6·2. Calc. for $C_{15}H_{18}O_6$: C, 61·2; H, 6·2%), $\lambda_{max.}$ (in EtOH) 270—280 mμ (log ε 1·66), $\nu_{max.}$ (in Nujol) 1730, 1700sh cm.$^{-1}$.

The methyl ester, prepared with methyl iodide and potassium carbonate, formed colourless prisms (from ether), m. p. 119°, not depressed when mixed with the ketone produced by oxidation of dimethyl shellolate with manganese dioxide. The infrared spectra were identical.

*Reaction of N-Bromosuccinimide with Dimethyl Shellolate.*—A solution of dimethyl shellolate (970 mg.), *N*-bromosuccinimide (530 mg.), and pyridine (400 mg.) in carbon tetrachloride (20 c.c.) was heated at 60—70° for 4 hr. The recovered gum (890 mg.) partly crystallised in ether. The crystalline fraction (490 mg.) was chromatographed on alumina (Brockman grade II); elution with ether afforded the ketone (IV; R = R′ = H) (212 mg.), m. p. 119—120° alone or mixed with the neutral product from oxidation of dimethyl shellolate by manganese dioxide. The infrared spectra were identical. Further elution with chloroform gave dimethyl shellolate (150 mg.). The non-crystalline fraction was separately chromatographed on alumina (grade II). Elution with ether afforded first a fraction (200 mg.) from which the *bromo-ketone* (IV: R = H, R′ = Br) was obtained as plates (from methanol), m. p. 177—178° (Found: C, 50·7; H, 5·0. $C_{17}H_{21}BrO_6$ requires C, 50·9; H, 5·3%). Further elution with ether gave another fraction (30 mg.) from which the ketone (IV; R = R′ = H) was obtained by cystallisation from ether.

The bromo-ketone was also obtained, in high yield, when dimethyl shellolate (0·324 g.), *N*-bromosuccinimide (0·178 g.), and a few crystals of benzoyl peroxide in carbon tetrachloride (10 c.c.) were heated on the water bath. There was a vigorous reaction and hydrogen bromide was evolved. The bromo-ketone was isolated by chromatography on alumina. This substance did not react with silver nitrate and was recovered after being heated with silver acetate in acetic acid.

We are indebted to Dr. B. S. Gidvani and Messrs. W. F. Rhodes and Co. Ltd. for generous gifts of " sticlac," and to Dr. G. Eglinton for some of the infrared spectra.

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## 1039. *Silyl Ethers of Tetrahydro-2-hydroxymethylpyran.*

By S. A. BARKER, J. S. BRIMACOMBE, M. R. HARNDEN, and M. STACEY.

Some silyl ether derivatives of tetrahydro-2-hydroxymethylpyran are reported. Toluene-*p*-sulphonylation and vinylation of tetrahydro-2-hydroxymethylpyran, and some derivatives of these compounds, have also been investigated.

RECENT publications [1] have shown the importance of the reaction of silicon-containing compounds with carbohydrates. Hedgley and Overend [1] and Schwarz *et al.*[2] synthesised trimethylsilyl derivatives of some mono- and di-saccharides and recorded their properties. Chang and Hass [3] and Henglein *et al.*[4] independently prepared octa-*O*-(trimethylsilyl)-sucrose. The trimethylsilyl derivatives are generally hydrolysed slowly in moist air and rapidly and quantitatively in boiling aqueous methanol.[1]

The complex nature of the products from sucrose and some alkylchlorosilanes, for example, dimethyldichlorosilane, prompted an investigation of the reaction of some aryl- and alkyl-chlorosilanes with tetrahydro-2-hydroxymethylpyran as model. Other workers [5] have shown that where preferential substitution of the sucrose molecule occurs this involves mainly the primary hydroxyl groupings, although a mixture of products usually results. Thus toluene-*p*-sulphonylation of sucrose with 3 mol. of reagent affords a mixture from which di-, tri-, and tetra-substituted derivatives have been isolated.[5]

Silyl ethers of tetrahydro-2-hydroxymethylpyran (see Table) were prepared essentially by the method described by Henglein *et al.*[4]. In the case of the ether derived from triphenylchlorosilane separation from hexaphenyldisiloxane was necessary. The infrared spectra of the products were in accordance with the proposed structures,[6] showing strong absorptions at 1020—1090 cm.$^{-1}$ (Si–O–C), 1090—1130 cm.$^{-1}$ (Si–Ph), 1250, 841, 754—756 ($SiMe_3$), 1259, 800—814 cm.$^{-1}$ ($SiMe_2$, SiMe).

Tetrahydro-2-tosyloxymethylpyran was prepared according to the method of Eglinton, Jones, and Whiting.[7] Treatment of this compound with sodium iodide in acetone [8] at 100° during 5 hr. afforded tetrahydro-2-iodomethylpyran in high yield. Attempts to cause tetrahydro-2-iodomethylpyran to react with sodium acetylide in liquid ammonia were unsuccessful. This is not wholly due to the low solubility of the iodo-compound in

[1] Hedgley and Overend, *Chem. and Ind.*, 1960, 378; Sprung, *J. Org. Chem.*, 1958, **23**, 58; Sprung and Nelson, *ibid.*, 1955, **20**, 1770; Burkhard, Schmitz, and Burnett, *J. Amer. Chem. Soc.*, 1953, **75**, 5957; Burkhard, *J. Org. Chem.*, 1957, **22**, 592; Langer, Connell, and Wender, 1958, **23**, 50; Henglein, *Angew. Chem.*, 1958, **70**, 510.
[2] Schwarz, Baronetsky, and Schoeller, *Angew. Chem.*, 1956, **68**, 335.
[3] Chang and Hass, *J. Org. Chem.*, 1958, **23**, 773.
[4] Henglein, Abelsnes, Heneka, Lienhard, Nakhre, and Scheinost, *Makromol. Chem.*, 1957, **24**, 1.
[5] Lemieux and Barrette, *Canad. J. Chem.*, 1960, **38**, 656.
[6] Bellamy, " Infrared Spectra of Complex Molecules," Methuen, p. 334.
[7] Eglington, Jones, and Whiting, *J.*, 1952, 2873.
[8] Tipson, Clapp, and Cretcher, *J. Org. Chem.*, 1947, **12**, 133.

liquid ammonia since no reaction was discernible on addition of ether and dimethylformamide; lithium acetylide [9] similarly did not react.

Mikhant'ev and Lapenko [10] recently prepared vinyl ethers of glucose derivatives by the direct action of acetylene under pressure in the presence of potassium hydroxide at 150—160°. Under similar conditions tetrahydro-2-vinyloxymethylpyran has been obtained in ~44% yield. An alternative route to this vinyl ether involved vinyl-exchange between tetrahydro-2-hydroxymethylpyran and butyl vinyl ether in the presence of mercuric acetate.[11]

An equimolar mixture of the vinyl ether and tetrahydro-2-hydroxymethylpyran in the presence of a trace of hydrochloric acid gave the acetal, 1,1-bis(tetrahydropyran-2-ylmethoxy)ethane. Similar reactions between vinyl ethers and alcohols have been recorded before.[12] Acidic hydrolysis of the acetal yielded acetaldehyde (detected with 4-hydroxybiphenyl) and tetrahydro-2-hydroxymethylpyran.

Reaction of diphenyldichlorosilane with glucose has been shown [4] to yield a polydiphenylsilylglucose. Our results also suggest that certain alkyl- and aryl-chlorosilanes might prove useful cross-linking agents for linear polymers such as cellulose. The mild conditions used in transvinylation might prove useful in the synthesis of vinylated sugar derivatives analogous to those prepared by Mikhant'ev and Lapenko.[10]

## Experimental

Silyl ethers were prepared under anhydrous conditions.

*Preparation of Silyl Ethers.*—The *ethers* (Table), with the exception of that derived from triphenylchlorosilane, were prepared as follows. A solution of dimethyldichlorosilane (12·3 g.) in dry hexane (30 ml.) was added during 20 min. to a stirred solution of tetrahydro-2-hydroxymethylpyran (28 g.) in pyridine (100 ml.). The solution was then cooled and shaken at room

Silyl ethers of tetrahydro-2-hydroxymethylpyran.

| No. | Silanes | Yield (%) | B. p./mm. | $n_D$ | Formula |
|---|---|---|---|---|---|
| 1 | Trimethyl(tetrahydropyran-2-ylmethoxy) ..... | 71 | 75—76°/14 | 1·4320 | $C_9H_{20}O_2Si$ |
| 2 | Dimethylbis(tetrahydropyran-2-ylmethoxy) ... | 80 | 134—136°/1·5 | 1·4571 | $C_{14}H_{28}O_4Si$ |
| 3 | Methyltris(tetrahydropyran-2-ylmethoxy) ..... | 74 | 170—172°/0·2 | 1·4683 | $C_{19}H_{36}O_6Si$ |
| 4 | (Tetrahydropyran-2-ylmethoxy)triphenyl ..... | 59 | (M. p. 52—53°) | | $C_{24}H_{26}O_2Si$ |
| 5 | Bis(tetrahydropyran-2-ylmethoxy)diphenyl ... | 85 | 224—228°/1 | 1·5380 | $C_{24}H_{32}O_4Si$ |
| 6 | Tris(tetrahydropyran-2-ylmethoxy)phenyl..... | 79 | 216—218°/0·05 | 1·5014 | $C_{24}H_{38}O_6Si$ |
| 7 | Tetrakis(tetrahydropyranylmethoxy) ..... | 77 | 234—236°/1 | 1·4725 | $C_{24}H_{44}O_8Si$ |

| | Found | | | | Required | | |
|---|---|---|---|---|---|---|---|
| No. | C (%) | H (%) | $M$ [a] | Formula | C (%) | H (%) | $M$ |
| 1 | 57·5 | 10·75 | 185 | $C_9H_{20}O_2Si$ | 57·4 | 10·7 | 188 |
| 2 | 58·1 | 9·9 | 284 | $C_{14}H_{28}O_4Si$ | 58·3 | 9·7 | 288 |
| 3 | 58·5 | 9·1 | 384 | $C_{19}H_{36}O_6Si$ | 58·8 | 9·3 | 389 |
| 4 | 77·2 | 7·0 | 369 | $C_{24}H_{26}O_2Si$ | 77·0 | 6·95 | 374 |
| 5 | 70·0 | 7·8 | 420 | $C_{24}H_{32}O_4Si$ | 70·0 | 7·8 | 413 |
| 6 | 64·1 | 8·3 | 440 | $C_{24}H_{38}O_6Si$ | 64·0 | 8·4 | 451 |
| 7 | 59·2 | 9·25 | 498 | $C_{24}H_{44}O_8Si$ | 59·0 | 9·0 | 489 |

[a] Determined by Barger's method.

temperature for 20 hr. Pyridine hydrochloride was removed and the filtrate concentrated under reduced pressure. The residue was distilled, yielding *dimethylbis(tetrahydropyran-2-ylmethoxy)silane* (21·8 g.), b. p. 134—136°/1·5 mm., $n_D^{18}$ 1·4571 (Found: C, 58·1; H, 9·9. $C_{14}H_{28}O_4Si$ requires C, 58·3; H, 9·7%).

*Tetrahydropyran-2-ylmethoxytriphenylsilane.*—A solution of triphenylchlorosilane (32·6 g.,

[9] Raphael, " Acetylenic Compounds in Organic Synthesis," London, 1955, p. 197.
[10] Mikhant'ev and Lapenko, *Zhur. obshchei Khim.*, 1957, **27**, 2840, 2972.
[11] Watanabe and Conlon, *J. Amer. Chem. Soc.*, 1957, **79**, 2828.
[12] Schostakowsky and Gershtein, *J. Gen. Chem.* (*U.S.S.R.*), 1946, **16**, 937.

0·11 mole) in dry pyridine (100 ml.) was added during 15 min. to a stirred solution of tetrahydro-2-hydroxymethylpyran (12 g., 0·103 mole) in dry pyridine (50 ml.). After refluxing for 4 hr. under anhydrous conditions, the mixture was shaken during 20 hr. The solution was filtered and concentrated under reduced pressure and the solid residue extracted with 7 : 10 v/v toluene–light petroleum (b. p. 40—60°) (85 ml.). The residual solid (2·2 g.) was washed with ether (100 ml.) and methanol (100 ml.) and after drying, had m. p. 223—224°. Its infrared spectrum was identical with that of hexaphenyldisiloxane (lit.,[13] m. p. 221—222°) (Found: C, 80·7; H, 5·7. Calc. for $C_{36}H_{30}OSi_2$: C, 80·9; H, 5·7%). The filtrate and washings were concentrated and on distillation yielded *tetrahydropyran-2-ylmethoxytriphenylsilane* (23 g.), b. p. 234—236°/5 mm., m. p. 52—53° (Found: C, 77·2; H, 7·0. $C_{24}H_{26}O_2Si$ requires C, 77·0; H, 6·95%).

*Tetrahydro-2-tosyloxymethylpyran.*—This was prepared essentially by the method described [7] and had m. p. 69—70° (lit.,[7] m. p. 72·5°).

*Tetrahydro-2-iodomethylpyran.*—Tetrahydro-2-tosyloxymethylpyran (4·2 g.) was treated with sodium iodide (8·5 g.) in acetone at 100° during 5 hr. in a sealed tube. The sodium toluene-*p*-sulphonate which separated from the cooled solution was removed and the filtrate diluted with water (*ca.* 150 ml.) and extracted with chloroform (3 × 150 ml.). The combined extracts were washed successively with potassium iodide solution and water and dried ($Na_2CO_3$). The residue after concentration was shaken with mercury to remove residual iodine and then taken up in a little chloroform and dried ($Na_2CO_3$). The solvent was removed; the *product* (3·3 g.) had b. p. 60—64°/6 mm., $n_D^{24}$ 1·5341 (Found: C, 31·6; H, 4·8. $C_6H_{11}IO$ requires C, 31·9; H, 4·9%).

*Vinylation of Tetrahydro-2-hydroxymethylpyran.*—(a) *By acetylene.* A rapid stream of acetylene was passed for 2 hr. through tetrahydro-2-hydroxymethylpyran (27·4 g.) containing potassium hydroxide (3 g.) at 150—160°. The cooled mixture was extracted with ether (5 × 50 ml.), and the extract washed with water (5 × 10 ml.) until the washings were no longer alkaline, and dried ($MgSO_4$). Removal of the solvent under nitrogen gave the vinyl ether admixed with starting material. A portion (8·6 g.) of this residue was chromatographed in light petroleum (b. p. 40—60°) on aluminium oxide (300 g.). Thereafter the desired *product* (2·9 g.) was obtained as a colourless liquid, $n_D^{22}$ 1·4540, with no absorption at *ca.* 3600 cm.$^{-1}$. The percentage unsaturation as determined by iodine titration was 93% (Found: C, 67·9; H, 9·95. $C_8H_{14}O_2$ requires C, 67·6; H, 9·9%).

(b) *By transvinylation.* A suspension of mercuric acetate (0·63 g.) in tetrahydro-2-hydroxymethylpyran (5·1 g., 0·044 mole) and butyl vinyl ether (37·2 g., 0·364 mole) was heated under reflux at 125° for 6 hr. Anhydrous potassium carbonate (5 g.) was added to the cooled mixture which was distilled under a reduced pressure of nitrogen directly from the carbonate. The fraction (4·7 g.), b. p. 56—60°/14 mm., was collected and distilled three times from metallic sodium, to yield the product (0·8 g.), b. p. 64°/20 mm., $n_D^{20·5}$ 1·4544. The percentage unsaturation as determined by iodine titration was 97% (Found: C, 67·9; H, 9·95%).

*1,1-Bis(tetrahydropyran-2-ylmethoxy)ethane.*—A crude sample of the above vinyl ether (1 g., 79% unsaturation) was added to tetrahydro-2-hydroxymethylpyran (0·83 g.) with cooling to 0°, and one drop of concentrated hydrochloric acid was added. After 24 hr. the mixture was distilled, to give the *product* (0·54 g.), b. p. 176°/20 mm., $n_D^{19}$ 1·4654 (Found: C, 64·9; H, 10·1. $C_{14}H_{26}O_4$ requires C, 65·1; H, 10·15%).

The dry acetal (0·15 g.) was treated under reflux with 2N-hydrochloric acid for 2 hr. The cooled hydrolysate gave a characteristic violet colour with 4-hydroxybiphenyl in concentrated sulphuric acid, indicating presence of acetaldehyde. The reaction mixture was extracted with ether (3 × 20 ml.) and dried ($K_2CO_3$). The liquid remaining after removal of the solvent had the infrared spectrum of tetrahydro-2-hydroxymethylpyran.

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[13] Dilthey and Eduardoff, *Ber.*, 1904, **37**, 1139; Schumb and Saffer, *J. Amer. Chem. Soc.*, 1941, **63**, 93.

# 1040. *A Comparison of the Nucleophilic Reactivity of Ethoxide, Methoxide, and Hydroxide Ions in Dioxan.*

By (Miss) I. R. Alet and B. D. England.

By an extrapolation procedure, the rates of the $S_N2$ reactions of sodium ethoxide, sodium methoxide, and sodium hydroxide with methyl iodide have been determined in 100% dioxan. The results show that the rates differ less in dioxan than they do in ethanol, methanol, and water, respectively. The results are compared with those of other workers who used a different solvent and substrate. Literature values for the rates of bimolecular substitutions of these reagents in their corresponding solvents are quoted and the reactivity of the hydroxide ion is discussed.

Although ethoxides, methoxides, and hydroxides are among the most widely used nucleophilic reagents, few comparisons of their nucleophilic reactivity under identical conditions have been reported. This is undoubtedly due partly to their strongly basic properties and partly to the virtual insolubility of the salts in aprotic solvents.

The first consideration precludes the use of simple kinetic measurements in hydroxylic solvents as a method of comparison, for proton transfer of the type $ROH + R'O^- \rightleftharpoons RO^- + R'OH$ would partly convert the added alkoxide or hydroxide into the conjugate base of the solvent.[1,2] A comparison of the rates of reaction of $RO^-$ and $R'O^-$ then requires a knowledge of the equilibrium concentration ratio of the two nucleophilic reagents and of the proportions of products arising from their attack on a common substrate. A study of this general type has been made by Bender and Glasson[3] using (*a*) acetyl-L-phenylalanine methyl ester in alkaline methanol–water and (*b*) the ethyl ester in alkaline ethanol–water. By extrapolation of both series of results to 100% water, the relative

Table 1.

Second-order rate constants (in l. mole$^{-1}$ sec.$^{-1}$) for $S_N2$ reactions of methyl iodide in various solvents.

MeI = *ca.* 0·01M; NaOR, NaOH = *ca.* 0·02M, throughout.

| Reagent | "Volume %" dioxan in solvent | 60 | 70 | 80 | 100 |
|---|---|---|---|---|---|
| NaOEt | Remainder | EtOH | EtOH | EtOH | — |
| | $10^3k_2$ at 35·2° | 6·33 | 7·00 | 7·85 | 9·4[a] |
| NaOMe | Remainder | MeOH | MeOH | MeOH | — |
| | $10^3k_2$ at 35·2° | 3·93 | 4·45 | 4·99 | 6·0[a] |
| NaOH | Remainder | $H_2O$ | $H_2O$ | $H_2O$ | — |
| | $10^3k_2$ at 70·0° | 12·5 | 13·3 | 13·9 | 15[a] |
| NaOH | Remainder | $H_2O$ | $H_2O$ | $H_2O$ | — |
| | $10^3k_2$ at 51·2° | 3·97 | 4·25 | 4·70 | 5·4[a] |
| NaOH | Remainder | $H_2O$ | $H_2O$ | $H_2O$ | — |
| | $10^3k_2$ at 35·2° | 1·34[b] | 1·45[b] | 1·69[b] | 2·0[c] |

[a] Value obtained by linear extrapolation of the (almost linear) plot of $k_2$ against the "volume %" of dioxan in the solvent. The extrapolated values are substantially unaltered if log $k_2$ is plotted against "volume %" of dioxan. [b] Value obtained by extrapolation assuming the Arrhenius equation $k_2 = A \exp(-E/RT)$: energies of activation for sodium hydroxide in 60, 70, 80, and 100% dioxan are, respectively, 13·4, 13·4, 12·7, and 12 kcal. mole$^{-1}$. [c] The same value $2·0 \times 10^{-3}$ is obtained either by extrapolation of results in the last row or of the third and fourth results in the final column.

rates were found to be 1 : 1·59 : 4·17 for hydroxide, methoxide, and ethoxide, respectively, the change of substrate from a methyl to an ethyl ester of the same acid being assumed to have no effect on the relative rates of hydrolysis.

The second consideration rules out hydrocarbons and ethers as reaction media, and

[1] (a) England, *Chem. and Ind.*, 1954, 1145; (b) Burns and England, *Tetrahedron Letters*, 1960, 24, 1.
[2] Baker and Neale, *J.*, 1954, 3225.
[3] Bender and Glasson, *J. Amer. Chem. Soc.*, 1959, **81**, 1590.

intermediate types of solvent such as ketones and esters will obviously be unsuitable with such alkaline reagents.

To overcome this problem we have employed a series of solvents consisting largely of dioxan (the remainder being ethanol, methanol, or water) to dissolve low concentrations of sodium ethoxide, methoxide, or hydroxide and have measured the rates of the $S_N2$ reactions of methyl iodide with these bases. A short extrapolation of the observed rates to 100% dioxan then gives a comparison of the nucleophilic reactivities in the same solvent. Methyl iodide was chosen as substrate because data on the nucleophilic power of reagents in the $S_N2$ reactions of aliphatic halides, as opposed to the bimolecular nucleophilic substitution of suitably activated aromatic halides,[4,5] are somewhat scanty. Also, with methyl iodide, complications due to the simultaneous occurrence of $S_N1$ reactions or eliminations are most unlikely. Results are assembled in Table 1.

## Experimental

*Reagents and Solutions.*—Methyl iodide was distilled and stored over silver wire in the dark. Standard solutions were prepared by weighing the iodide. "AnalaR" ethanol and methanol and distilled water free from carbon dioxide were used to make up the solvents. The alkoxide solutions were prepared by adding pieces of clean sodium to the appropriate solvents containing dioxan and methanol or ethanol. With aqueous solvents, "AnalaR" sodium hydroxide was added after being washed to remove carbonate from the surface of the pellets. Alkaline solutions were standardised by titration in a nitrogen atmosphere, Bromothymol Blue being used. Considerable difficulty was experienced with the purification of dioxan when used with sodium hydroxide (see below).

*Mixed solvents.* The term "60 volume %" of dioxan indicates that $6x$ volumes of dioxan were mixed with $4x$ volumes of ethanol, methanol, or water at 20°.

*Kinetic Measurements.*—Aliquot parts of reaction mixtures were added to dilute nitric acid, and iodide ion was titrated potentiometrically with 0·01N-silver nitrate. The runs in dioxan–methanol and dioxan–ethanol were carried out in glass vessels at 35·2°, about 15 aliquot parts being analysed in each run. In all cases at least 75% of the reaction was followed. Individual constants showed a maximum deviation of 4% from the mean and duplicate runs were reproducible to within 1%. In 80% dioxan–20% methanol as solvent, sodium iodide crystallised during the reaction and the sealed-tube technique was adopted in this case. Solubility difficulties prevented use of solvents containing 90% of dioxan.

When 60% dioxan–40% water was used as solvent for reactions with sodium hydroxide, the following observations were made: (*a*) With methyl iodide alone in the solvent at 80° in glass vessels, the first-order constant for the solvolysis of methyl iodide showed a continuous downward drift and an average value of about $2 \times 10^{-5}$ sec.$^{-1}$. (*b*) When sodium hydroxide was used alone under the conditions in (*a*), there was a continuous fall in titre. (*c*) When the solvent contained methyl iodide (*ca.* 0·01M) and sodium hydroxide (*ca.* 0·02M) at 51·2° in glass vessels, the second-order constant showed a continuous downward drift.

These results were probably due to a combination of attack of reagents, particularly hydroxide ion, on the glass and on the dioxan. Similar difficulties have been noted by other workers.[4,6,7] The "AnalaR" dioxan was purified by Vogel's method and stored under nitrogen, and the reactions were carried out in Polythene bottles at 70° and 51·2° because of the low velocity at 35·2°. Under these conditions, good second-order constants were obtained showing a maximum and random deviation of about 6% from the mean for at least 60% of the reaction. The mean value was reproducible to within 1·5%. Polythene disintegrates after a few days in a thermostat bath at 60° with a surface layer of paraffin to prevent evaporation. Rates at 35·2° were obtained by extrapolation (Table 1).

*Interference from Solvolysis of Methyl Iodide in Aqueous Media.*—The kinetics of hydrolysis of methyl iodide in pure water, with and without added hydroxide, have been extensively

[4] Bunnett and Davis, *J. Amer. Chem. Soc.*, 1954, **76**, 3011; 1958, **80**, 4337.
[5] Bevan and Hirst, *J.*, 1956, 254.
[6] Fairclough and Hinshelwood, *J.*, 1937, 538.
[7] Foster and Hammett, *J. Amer. Chem. Soc.*, 1946, **68**, 1736; Beste and Hammett, *J. Amer. Chem. Soc.*, 1940, **62**, 2481.

studied by Moelwyn-Hughes.[8] The solvolytic reaction occurring concurrently when hydroxide is added should cause a slight upward drift of the observed second-order constants. In dioxan–water, interference by water solvolysis should be less serious for the following reasons: (*a*) the water concentration is reduced; (*b*) the rate of the solvolytic reaction (between two uncharged reagents) should, according to Hughes and Ingold's theory of solvent action,[9] decrease as more dioxan is added; and (*c*) for the same reason the rate of substitution by hydroxide ion should increase.

At 70°, the specific rate ratio, $k_2/k_1$, for substitution by hydroxide ion and for solvolysis in pure water is about 300, whereas from our results, the same ratio in 60% dioxan–40% water is about 1700. However, the relative proportions of these reactions depend also on the concentration of sodium hydroxide, an increased proportion of solvolysis occurring at lower concentrations. We have calculated that the percentage of solvolysis occurring under our conditions was never more than 3%, and no corrections for this effect were made.

## Discussion

The results in Table 1 give the relative rates 1 : 3·0 : 4·7 for hydroxide, methoxide, and ethoxide, respectively, reacting with methyl iodide in dioxan at 35·2° c. With mixed solvents the rate is increased slightly in all cases by increasing the proportion of dioxan in the mixture, an observation which is in agreement with the predictions of Hughes and Ingold's theory of solvent action. It is noteworthy, however, that a qualitatively opposite result was obtained for the reaction of allyl chloride with potassium hydroxide (*ca.* 0·17M) in 40% and 60% aqueous dioxan at 64·9° (where the rate is twice as fast in the more aqueous solvent) by Vernon [10] who attributed the anomaly to the greater polarity of the transition state in $S_N2$ substitutions of allyl halides.

From rates and Arrhenius parameters quoted by Moelwyn-Hughes,[8,11] the rates of reaction of methyl iodide with hydroxide in water, methoxide in methanol, and ethoxide in ethanol are found to be $2{\cdot}15 \times 10^{-4}$, $9{\cdot}08 \times 10^{-4}$, and $3{\cdot}14 \times 10^{-3}$ l. mole$^{-1}$ sec.$^{-1}$, respectively (ratio 1 : 4·22 : 14·6) at 35·2°. These are all less than the values in Table 1 for 60% dioxan–40%-water, -methanol, or -ethanol, and it seems likely that the rate of the reaction of each of these anions with methyl iodide shows a continuous increase as the solvent is changed from pure water, methanol, or ethanol to pure dioxan. However, the rate changes by different factors over the complete range of solvent variation in the three cases: 9·3 for the change of water, 6·6 for the change of methanol, and 3·0 for the change of ethanol to pure dioxan in each case. Again this is qualitatively the expected result if the polarity order is water > methanol > ethanol.

In Table 2 a critical selection of literature data on the relative rates of attack of ethoxide and methoxide ions, dissolved in their parent solvents, on various halides is assembled. Data for the attack of hydroxide ion in water on halides are meagre because of solubility difficulties and are not included. The rate ratio is always greater than in dioxan, as expected, and seems very roughly constant over a wide range of halides. Insofar as there are differences between halides these seem to bear no systematic relation to their structure.

There is surprisingly close agreement between the values obtained by us (1 : 3·0 : 4·7) for the relative reactivity of hydroxide, methoxide, and ethoxide and those of Bender and Glasson [3] (1 : 1·59 : 4·17), for the two sets of results refer to different substrates and, especially, to different solvents, dioxan and water, which are at opposite ends of the polarity scale. Nevertheless it would be unwise, in our opinion, to infer that the nucleophilic reactivity of hydroxide ion is never less than that of methoxide by a factor of more than three or of ethoxide by more than five. There is good evidence [4] for the low reactivity of hydroxide in its reaction with 1-chloro-2,4-dinitrobenzene in dioxan–water and we have

[8] Moelwyn-Hughes, *Proc. Roy. Soc.*, 1949, *A*, **196**, 540; 1953, *A*, **220**, 386.
[9] Ingold, " Structure and Mechanism in Organic Chemistry," Cornell, Ithaca, N.Y., 1953, p. 347.
[10] Vernon, *J.*, 1954, 4462.
[11] Moelwyn-Hughes, " Physical Chemistry," Pergamon, London, 1957, p. 1208.

TABLE 2.

Rates of reaction of halides with ethoxide in ethanol and methoxide in methanol. Rate constants (in l. mole$^{-1}$ sec.$^{-1}$) have been calculated at 25° c from Arrhenius parameters wherever possible.

| Halide | Ethoxide in ethanol | | | Methoxide in methanol | | | Rate factor |
|---|---|---|---|---|---|---|---|
| | $t$ (° c) | $k_2$ | Ref. | $t$ (° c) | $k_2$ | Ref. | |
| Methyl iodide | 25 | $1{\cdot}10 \times 10^{-3}$ | 11 | 25 | $2{\cdot}55 \times 10^{-4}$ | 11 | 4·32 |
| Methyl bromide | 25 | $1{\cdot}57 \times 10^{-3}$ | 12 | 25 | $2{\cdot}86 \times 10^{-4}$ | 11 | 5·49 |
| Ethyl iodide | 70·2 | $1{\cdot}51 \times 10^{-2}$ | 13 | 70·2 | $6{\cdot}83 \times 10^{-3}$ | 1(a) | 2·22 |
| *o*-Fluoronitrobenzene | 25 | $9{\cdot}2 \times 10^{-4}$ | 14 | 25 | $1{\cdot}16 \times 10^{-4}$ | 15 | 7·93 |
| *p*-Fluoronitrobenzene | 25 | $8{\cdot}13 \times 10^{-4}$ | 16 | 25 | $2{\cdot}14 \times 10^{-4}$ | 16 | 3·80 |
| *o*-Chloronitrobenzene | 25 | $7{\cdot}5 \times 10^{-7}$ | 17 | 25 | $1{\cdot}2 \times 10^{-7}$ | 18 | 6·25 |
| *p*-Chloronitrobenzene | 25 | $1{\cdot}84 \times 10^{-6}$ | 19 | 25 | $4{\cdot}0 \times 10^{-7}$ | 18 | 4·60 |
| 1-Chloro-2,4-dinitrobenzene | 25 | $8{\cdot}08 \times 10^{-2}$ | 16 | 25 | $2{\cdot}6 \times 10^{-2}$ | 16 | 3·11 |
| 1-Fluoro-2,4-dinitrobenzene | 0 | 8·97 | 16 | 0 | 1·85 | 16 | 4·85 |
| 1-Chloro-2,6-dinitrobenzene | 50 | $1{\cdot}47 \times 10^{-3}$ | 20 | 50 | $7{\cdot}37 \times 10^{-3}$ | 18 | 2·00 |

evidence [21] for a rate ratio of about 20 in the reaction of hydroxide and methoxide with the same aromatic halide in methanol–water. The nucleophilic reactivity of hydroxide in water towards ethylene oxide [22] is also exceptionally small.

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[12] Dostrovsky and Hughes, *J.*, 1946, 157.
[13] Fraser, M.Sc. Thesis, Wellington, N.Z., 1956.
[14] Bevan, *J.*, 1953, 655.
[15] Rouche, *Bull. Sci. Acad. roy. Belg.*, 1921, 534; "Tables of Chemical Kinetics," 1954 Suppl., National Bureau of Standards, Washington, D.C., p. 243.
[16] Burns, M.Sc. Thesis, Wellington, N.Z., 1960.
[17] Riklis, *J. Gen. Chem. U.S.S.R.*, 1947, **17**, 1511.
[18] Miller and Williams, *J.*, 1953, 1475.
[19] Bevan, *J.*, 1951, 2340.
[20] Bevan, Hughes, and Ingold, *Nature*, 1953, **171**, 301.
[21] Alet, M.Sc. Thesis, Wellington, N.Z., 1958.
[22] Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co., New York, 1940, p. 302.

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## 1041. *The Hemicelluloses of Roselle Fibre* (Hibiscus sabdariffa).

By P. C. DAS GUPTA.

Roselle fibre holocellulose was extracted with alkaline solutions of successively increasing concentration and finally with alkaline borate solution. Hemicellulose fractions (1—4) were isolated from the solutions. Fractions 2 and 3 have molecular weights of 23,000 ± 500 and 33,600 ± 500, respectively. Analytical data are recorded for each fraction.

Partial acid hydrolysis of roselle hemicellulose yields (2-D-xylose 4-*O*-methyl-α-D-glucopyranosid)uronic acid. The main hemicellulose fraction (2) was methylated and then hydrolysed, affording 2,3,4-tri-, 2,3-di-, and 3-mono-*O*-methyl-D-xylose, and (3-*O*-methyl-2-D-xylose 2,3,4-tri-*O*-methyl-α-D-glucopyranosid)uronic acid in the approximate molar proportions 1 : 34·5 : 2·1 : 6·9. The methylated polysaccharide has a degree of polymerisation 124 ± 3. It is concluded that the polysaccharide is composed of chains of *ca.* 107 1,4-linked β-D-xylopyranose residues, approximately every sixth residue carrying a terminal 4-*O*-methyl-α-D-glucopyranosiduronic acid residue linked through position 2. A small degree of branching in the backbone of D-xylose residue is indicated.

THE structural studies of hemicelluloses of land plants [1] from different sources have revealed their general characteristics. The hemicelluloses of bast fibres so far studied were

[1] Aspinall, *Adv. Carbohydrate Chem.*, 1959, **14**, 429.

those from New Zealand flax,[2] from jute,[3] and from common flax.[4] Roselle fibre, a lignified tissue, is used as a substitute for jute. An attempt was made to fractionate the total carbohydrate constituent of roselle fibre, and this paper describes the structure of the main polysaccharide component of the hemicellulose fraction.

The extractive-free fibre was delignified by the chlorite method.[5] Stepwise extraction [6] (see Experimental section) of the resulting holocellulose led to four hemicellulose fractions (1—4) and a cellulose-rich residue (see Table). Fraction 2A was obtained by treatment of fraction 2 with Fehling's solution.

Physical constants of hemicellulose fractions.

| Fraction | Yield * (%) | Xylan † (%) | Uronic anhydride (%) | MeO (%) | Equiv. | D.P. | $[\alpha]_D$ (in N-NaOH) |
|---|---|---|---|---|---|---|---|
| 1 | 0·95 | 47·9 | 23·5 | 2·8 | 705 | — | −4·9° |
| 2 | 9·65 | 70·6 | 17·1 | 3·4 | 1071 | — | −46·9 |
| 2A | — | 76·6 | 17·5 | 3·6 | 1040 | 163 ± 3 | −46·6 |
| 3 | 6·74 | 65·2 | 16·6 | 3·2 | 1170 | 241 ± 3 | −37·7 |
| 4 | 1·39 | 50·4 | 13·4 | 2·8 | 1374 | — | −39·6 |

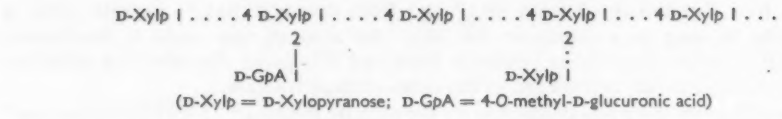
* On the weight of dry fibre. † Corrected for uronic anhydride [uronic anhydride gives 16·2% of its weight of furfuraldehyde (Sen and Das Gupta, unpublished work)].

Partial acid hydrolysis of roselle hemicellulose yields xylose and a main acidic component, characterised as (2-D-xylose 4-*O*-methyl-α-D-glucopyranosid)uronic acid.

Fraction 2 was converted into its fully methylated derivative which on hydrolysis gave 2,3,4-tri-, 2,3-di-, and 3-mono-*O*-methyl-D-xylose, and (3-*O*-methyl-2-D-xylose 2,3,4-tri-*O*-methyl-α-D-glucopyranosid)uronic acid in the approximate molar proportions 1 : 34·5 : 2·1 : 6·9. These results and the negative rotation of the original hemicellulose and its methylated derivative indicate that the polysaccharide contains a chain of 1,4-linked β-D-xylopyranose residues, approximately every sixth xylose residue carrying a terminal 4-*O*-methyl-D-glucuronic acid residue attached as a side chain to position 2. The methoxyl content, uronic anhydride content, and equivalent weight of roselle hemicellulose fraction (2A) also indicate the presence of approximately six xylose residues for each 4-*O*-methylglucuronic acid residue.

The number-average molecular weight of the methylated polysaccharide, as determined by osmometry, was found to be 20,800 ± 500 (degree of polymerisation, 124 ± 3). Since the methylation analysis indicated the presence of 2·5 non-reducing xylose end groups for a molecule of this size, there will be on the average 1·5 branches in the main chain of xylose residues per molecule. The corresponding figure for the original polysaccharide will be 2. The amount of formic acid liberated by periodate oxidation of fraction (2A) also suggests a number of branch points in the polysaccharide molecule. The presence of mainly 3-*O*-methylxylose as the monomethyl ether of xylose in the hydrolysis product of methylated hemicellulose indicates that the branch points must involve 1,2-linkages. The proportion of 3-*O*-methylxylose is slightly higher than could be accounted for the branch points and may arise from partial hydrolysis of the partially methylated aldobiouronic acid or incomplete methylation or demethylation during hydrolysis of the methylated polysaccharide. The accompanying partial structure for the xylan indicates the main features of the molecule. The consumption of 0·82 mol. of periodate per sugar residue also supports this structure.

[2] McIlroy, Holmes, and Mauger, *J.*, 1945, 796; McIlroy, *J.*, 1949, 121.
[3] (*a*) Sarkar, Mazumdar, and Pal, *Textile Res. J.*, 1952, **22**, 529; (*b*) Aspinall and Das Gupta, *J.*, 1958, 3627.
[4] Geerdes and Smith, *J. Amer. Chem. Soc.*, 1955, **77**, 3569, 3572.
[5] Chattopadhyaya and Sarkar, *Proc. Nat. Inst. Sci., India*, 1946, **12**, 23.
[6] Jones, Wise, and Jappe, *TAPPI*, 1956, **39**, 139.




(D-Xylp = D-Xylopyranose; D-GpA = 4-*O*-methyl-D-glucuronic acid)

Fraction 3 appears to have a structure similar to that of fraction 2 but a higher molecular weight. The major part of roselle hemicellulose thus consists of 4-*O*-methylglucuronoxylan whose structure is similar to that from jute [3] but differs from that of flax-straw hemicellulose [4] in having a higher proportion of uronic acid and in the absence of L-rhamnopyranose as the integral part of its molecule.

Roselle α-cellulose and the cellulose-residue both contain, besides glucose, a certain proportion of other sugars. It is not possible to ascertain with certainty whether they are associated with, or an integral part of, the cellulose molecule.

## Experimental

Paper partition chromatography was carried out on Whatman No. 1 and No. 3MM filter papers with the following solvent systems (v/v): (A) butan-1-ol–ethanol–water (40 : 11 : 19); (B) butan-1-ol–pyridine–water (10 : 3 : 3); (C) ethyl acetate–acetic acid–water (9 : 2 : 2); (D) butan-2-one, two-thirds saturated with water, containing 1% of ammonia; (E) benzene–ethanol–water (169 : 47 : 15, upper layer). Saturated aqueous solution of aniline oxalate was used as the spray reagent. Paper ionophoresis was in borate buffer at pH 10. Evaporations were carried out *in vacuo* at 40—45°.

*Composition of Roselle Fibre.*—Analysis by standard methods [7] indicated the following composition: α-cellulose 59·7, lignin 9·87, pentosan 15·0, Ac 4·76, ash 0·47, uronic anhydride 4·2, and fat and wax 0·58; residues of galactose 3·35, glucose 64·8, mannose 1·36, arabinose 0·42, rhamnose 0·77, and xylose 11·63%.

*Isolation and Purification of the Hemicellulose Fractions.*—Roselle fibre, in small pieces, was extracted with 1 : 2 v/v alcohol–benzene. The extractive-free fibre was delignified with sodium chlorite to give holocellulose [90·0%; lignin (Schwalbe's), 3·0; Ac, 4·7%). The holocellulose (450 g.) was treated successively with 10 parts of 2% sodium carbonate solution, 4% and 10% sodium hydroxide solution, and 16% sodium hydroxide solution containing 4% of boric acid for 48, 2, 2, and 72 hr., respectively. Hemicellulose fractions (1—4) were isolated from the solutions as described previously.[3a] Hemicellulose fraction 1 was brown owing to the presence of lignin. It was purified to a white powder by treatment with sodium chlorite in hot methanol.[8] Fraction 2 (10 g.) was treated thrice with Fehling's solution according to the method of Chanda *et al.*,[9] giving fraction 2A (8·6 g.).

Samples of the hemicellulose fractions, cellulose residue, and α-cellulose were hydrolysed as described by Saeman *et al.*,[10] and the neutral sugars in the hydrolysate were estimated by quantitative paper chromatography [11] with solvents B and C. The results are summarised in the Table.

| Fraction | A | Gal | Glu | Xyl | Man | Rham |
|---|---|---|---|---|---|---|
| 1 | 2·5 | 7·7 | 0·55 | 82·5 | — | 6·7 |
| 2 | 0·6 | 1·2 | 0·6 | 96·4 | — | 1·3 |
| 2A | — | — | 0·15 | 99·1 | — | 0·7 |
| 3 | — | 0·9 | 6·3 | 89·0 | 2·6 | 1·1[b] |
| 4 | — | 1·1 | 14·3 | 71·0 | 12·75 | 0·9 |
| Cellulose residue | — | — | 98·45 | 1·1 | 0·3 | 0·2 |
| α-Cellulose | — | — | 95·7 | 3·7 | 0·4 | 0·1 |

*Isolation of the Aldobiouronic Acid.*—The hemicellulose (mixture of fractions 2 and 3; 60 g.) was heated with N-sulphuric acid (1800 ml.) at 100° for 7 hr. ($[\alpha]_D$ +39·6°, const.). The cooled solution was neutralised with barium hydroxide and barium carbonate, and the filtrate was

[7] Das Gupta, *J. Sci. Ind. Res., India*, in the press.
[8] Rogers, Mitchell, and Ritter, *Analyt. Chem.*, 1947, **19**, 1029.
[9] Chanda, Hirst, Jones, and Percival, *J.*, 1950, 1289.
[10] Saeman, Moore, Mitchell, and Millett, *TAPPI*, 1954, **37**, 336.
[11] Flood, Hirst, and Jones, *J.*, 1948, 1679.

concentrated to a small volume and then poured into ethanol. The precipitated barium salts were extracted with boiling ethanol until the extract was more or less free from xylose. The barium salts were then dissolved in water, barium ions were removed with Amberlite resin I.R.-120($H^+$), and the solution was concentrated to a syrup. Chromatography in solvent C showed a main component with $R_{xyl}$ 0·83. The acidic syrup (5·4 g.) was dissolved in a little water, absorbed on cellulose powder, and dried in a vacuum-desiccator, and the mixture was placed on a cellulose column (70 × 4·5 cm.).[12] Elution of the column with solvent C yielded a chromatographically pure aldobiouronic acid (1·4 g.), $[\alpha]_D^{25}$ +105° (*c* 1·0 in $H_2O$) (Found: OMe, 9·3%; equiv., 352. Calc. for $C_{12}H_{20}O_{11}$: OMe, 9·1%; equiv., 340).

*Characterisation of Aldobiouronic Acid as* (2-D-*Xylose* 4-O-*Methyl*-α-D-*glucopyranosid*)*uronic Acid.*—The aldobiouronic acid (0·4 g.) was refluxed with methanolic 2% hydrogen chloride, and the resulting methyl ester methyl glycoside was reduced with lithium aluminium hydride in tetrahydrofuran.[13] The product was hydrolysed with N-sulphuric acid at 100° for 7 hr. and, after neutralisation with barium carbonate, the sugars were separated on filter sheets with solvent A, giving fractions *a* and *b*. Chromatography of the sugar and the product of periodate oxidation [14] indicated that fraction *a* (190 mg.), $[\alpha]_D^{27}$ +61° (*c* 1·1 in $H_2O$) (Found: OMe, 15·5. Calc. for $C_7H_{14}O_6$: OMe, 16·0%), was 4-*O*-methyl-D-glucose. The derived glucosazone had m. p. and mixed m. p. 159—160°, $[\alpha]_D^{27}$ −17·4° (*c* 0·64 in EtOH) (Found: OMe, 8·6; N, 15·3. Calc. for $C_{19}H_{24}N_4O_4$: OMe, 8·3; N, 15·0%). Fraction *b* (142 mg.), m. p. and mixed m. p. (with D-xylose) 144°, $[\alpha]_D^{25}$ +18° (*c* 1·0 in $H_2O$), was characterised by conversion into the di-*O*-benzylidene dimethyl acetal, m. p. 210°, $[\alpha]_D^{30}$ −8·2° (*c* 0·5 in $CHCl_3$).

Treatment of the methyl ester methyl glycoside (760 mg.) of the aldobiouronic acid first with methyl sulphate and sodium hydroxide and then with methyl iodide and silver oxide gave the methylated derivative (700 mg.). This with lithium aluminium hydride in ether [13] and then methyl iodide and silver oxide furnished the fully methylated neutral disaccharide (475 mg.), $[\alpha]_D^{25}$ +109° (*c* 1·0 in $CHCl_3$) (Found: OMe, 52·0. Calc. for $C_{18}H_{34}O_{10}$: OMe, 52·9%). Hydrolysis of this (400 mg.) with N-sulphuric acid at 100° for 6 hr. yielded a syrup which was separated by paper chromatography with solvent A into two fractions. Fraction (i) (112 mg.) was 2,3,4,6-tetra-*O*-methyl-D-glucose, m. p. and mixed m. p. 88—90°, $[\alpha]_D^{30}$ +84° (equil.) (*c* 1·0 in $H_2O$) (Found: OMe, 51·9. Calc. for $C_{10}H_{20}O_6$: OMe, 52·5%). The 2,3,4,6-tetra-*O*-methyl-*N*-phenyl-D-glucopyranosylamine, after recrystallisation from light petroleum, had m. p. 135—136°, $[\alpha]_D^{30}$ +208° (*c* 0·5 in $COMe_2$). Chromatography with solvent E and ionophoresis of fraction (ii) (80 mg.) showed only 3,4-di-*O*-methyl-D-xylose, $[\alpha]_D^{30}$ +21·8° (*c* 1·1 in $H_2O$), characterised by conversion into 3,4-di-*O*-methyl-D-xylonolactone, m. p. 66—67°, $[\alpha]_D^{30}$ −22° (equil.) (*c* 1·0 in $H_2O$) (Found: OMe, 34·75. Calc. for $C_7H_{12}O_5$: OMe, 35·2%).

*Periodate Oxidation.*—Hemicellulose fractions 2A and 3 (900 mg.) were shaken with water (61 ml.) to form colloidal solutions, and 0·31M-sodium metaperiodate (29·5 ml.) was added. Oxidation was allowed to take place at 10° in the dark. The uptake of periodate, determined by the arsenite method, was constant after 268 hr. at values of 0·82 and 0·80 mol. of periodate consumed per sugar residue for fractions 2A and 3 respectively.

Oxidation of sodium salts of hemicellulose fractions 2A and 3 with potassium metaperiodate rapidly liberated one mole of formic acid per 4 kg. of hemicellulose in both cases in 150 hr.

*Methylation of Roselle Hemicellulose.*—The hemicellulose (fraction 2) (19 g.) was methylated by methyl sulphate and sodium hydroxide and then with methyl iodide and silver oxide, to give a methylated hemicellulose (20 g.), $[\alpha]_D^{25}$ −39° (*c* 1·0 in $CHCl_3$) (Found: OMe, 38·3%), whose infrared spectrum indicated the absence of hydroxyl groups. This (18 g.) was fractionated by dissolution in boiling chloroform–light petroleum (b. p. 60—65°). The main fraction (16·27 g.) was soluble in this mixture (3 : 7) and had $[\alpha]_D^{30}$ −43·8° (*c* 1·5 in $CHCl_3$) (Found: OMe, 39·0%). Hydrolysis of this fraction and quantitative chromatography [9] of the resulting neutral methylated sugars showed the tri-, di-, and mono-*O*-methylxylose in the proportion of 1 : 32 : 2.

*Hydrolysis of Methylated Hemicellulose and Separation of the Methylated Sugars.*—The methylated hemicellulose (8 g.) was hydrolysed successively with boiling methanolic 1·26% hydrogen chloride (700 ml.) for 10 hr. ($[\alpha]_D$ +86°, const.) and 0·5N-hydrochloric acid (700 ml.)

[12] Hough, Jones, and Wadman, *J.*, 1949, 2511; Whistler, Conrad, and Hough, *J. Amer. Chem. Soc.*, 1954, **76**, 1663.
[13] Abdel-Akher and Smith, *Nature*, 1950, **166**, 1037; Lythgoe and Trippett, *J.*, 1950, 1983.
[14] Lemieux and Bauer, *Canad. J. Chem.*, 1953, **31**, 814.

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at 100° for 8 hr. ($[\alpha]_D$ +52°, const.). The solution was neutralised with silver carbonate, silver ion removed with hydrogen sulphide, and the solution concentrated to a syrup (8·5 g.). The methylated sugars (6 g.) were fractionated on a cellulose column (75 × 4·5 cm.) by solvent D into three fractions (1—3); eluting the column with water gave a fourth fraction (containing barium salts), which was treated with Amberlite resin I.R.-120($H^+$) and concentrated to a syrup.

*Fraction* 1. Chromatography of the syrup (120·5 mg.) showed only 2,3,4-tri-*O*-methyl-D-xylose, m. p. and mixed m. p. 84—85°, $[\alpha]_D^{25}$ +19·5° (equil.) (*c* 0·5 in $H_2O$) (Found: OMe, 48·0. Calc. for $C_8H_{16}O_5$: OMe, 48·4%).

*Fraction* 2. The syrup (3·85 g.) crystallised when seeded with 2,3-di-*O*-methyl-β-D-xylose and, recrystallised from ether, had m. p. 91—92°, $[\alpha]_D^{21}$ −34° (3 min.) ⟶ +23·5° (60 min., const.) (*c* 1·5 in $H_2O$) (Found: OMe, 35·0. Calc. for $C_7H_{14}O_5$: OMe, 34·8%). The derived 2,3-di-*O*-methyl-*N*-phenyl-D-xylopyranosylamine, recrystallised from ethyl acetate, had m. p. 121°, $[\alpha]_D^{25}$ +181° (*c* 0·8 in EtOAc) (Found: OMe, 24·6. Calc. for $C_{13}H_{19}NO_4$: OMe, 24·5%), and 2,3-di-*O*-methyl-D-xylonamide had m. p. 131—132°, $[\alpha]_D^{29}$ +46·3° (*c* 1·1 in $H_2O$) (Found: OMe, 31·8. Calc. for $C_7H_{15}NO_5$: OMe, 32·1%).

*Fraction* 3. Chromatography and ionophoresis of the syrup (214·5 mg.), $[\alpha]_D^{30}$ +15·9° (*c* 0·67 in $H_2O$), showed 3-*O*-methyl-D-xylose and a trace of the 2-*O*-methyl ether (Found: OMe, 18·7. Calc. for $C_6H_{12}O_5$: OMe, 18·9%).

*Fraction* 4. Chromatography of the syrup (1·66 g.) in solvent C showed a main component and a trace of 2,3,4-tri-*O*-methylglucuronic acid. The syrup (550 mg.) was converted into its methyl ester methyl glycoside and then reduced in ether solution with lithium aluminium hydride in ether. The product (470 mg.) was hydrolysed with N-sulphuric acid at 100° for 7 hr. The hydrolysate on chromatography and ionophoresis showed 2,3,4-tri-*O*-methyl-D-glucose, 3-*O*-methyl-D-xylose, and traces of 2,3-di-*O*-methyl-D-xylose. The sugars were separated on filter sheets with solvent A into two main fractions *a* and *b*. Fraction *a* (236·7 mg.) was 2,3,4-tri-*O*-methyl-D-glucose, $[\alpha]_D^{30}$ +70·1° (*c* 1·2 in $H_2O$) (Found: OMe, 41·6. Calc. for $C_9H_{18}O_6$: OMe, 41·9%). The derived 2,3,4-tri-*O*-methyl-*N*-phenyl-D-glucosylamine had m. p. 143—144° (Found: OMe, 31·6. Calc. for $C_{15}H_{23}NO_5$: OMe, 31·3%). Fraction *b* (185·5 mg.) was shown by ionophoresis to be 3-*O*-methyl-D-xylose, $[\alpha]_D^{30}$ +14° (*c* 1·85 in $H_2O$) [derived 3-*O*-methyl-*N*-phenyl-D-xylosylamine had m. p. 135° (from ethyl acetate), $[\alpha]_D^{25}$ +81·3° (*c* 0·5 in EtOAc) (Found: OMe, 12·75; N, 5·6. Calc. for $C_{12}H_{17}NO_4$: OMe, 13·0; N, 5·9%).

*Molecular-weight Determinations.*—The number-average molecular weights of fractions 2A and 3 were determined by measuring the osmotic pressure of solutions of their sodium salts in 0·4M-aqueous sodium chloride.[15] The measurements were made by the static method at at 35° ± 0·02° with the Hellfritz osmometer [16] and a Gel Cellophane membrane. The molecular weight of the methylated hemicellulose was determined in butyl acetate with a membrane " Ultrazellafilter allerfeinst " supplied by Membrane Filter Gesellschaft, Göttingen.

The molecular weight of α-cellulose and cellulose residue were determined from the viscosity of their solutions in cuprammonium hydroxide by using the equation,[17] $[\eta] = 5 \times 10^{-4}M$. The measurements were made at 20° ± 0·05° in the British Cotton Industries Research Association standard capillary viscometer. The values obtained were 155,000 ± 1000 and 148,000 ± 1000 respectively.

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Lafayette, Indiana, U.S.A. [*Received, June 26th*, 1961.]

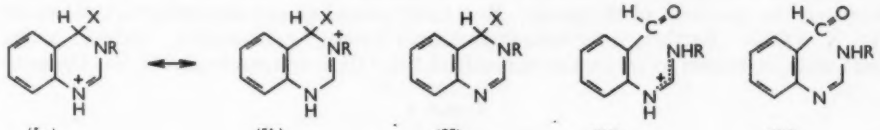
[15] Das, Das Gupta, and Basu, *J. Sci. Ind. Res., India*, 1953, **12**, *B*, 146.
[16] Hellfritz, *Makromol. Chem.*, 1951, **7**, 184.
[17] Staudinger and Daumiller, *Annalen*, 1937, **529**, 219.

# 1042. *Quinazolines. Part III.* The Structure of the Hydrated Quinazoline Cation.*

By Adrien Albert, W. L. F. Armarego, and E. Spinner.

The hydrated cation of quinazoline is shown to have the structure (I; X = OH, R = H) by comparison of its physical properties with those of the 3-methylquinazolinium ion and of the *pseudo*-base obtained from the latter. This base has been proved to have the constitution (II; X = OH, R = Me).

Quinazoline forms an abnormal cation in dilute aqueous acid.[1-3] Strong evidence was adduced [3] in support of structure (I; X = OH, R = H) for this ion, but its ultraviolet spectrum does not resemble that of the ion (I; X = R = H) as closely as would have been expected on this basis.[3] The infrared spectrum of solid quinazoline hydrochloride " monohydrate " did not yield conclusive structural information [3] and further evidence was desirable, preferably for a neutral molecule (II), so that no problem of the weighting of two contributing canonical forms, such as (Ia) and (Ib), could arise.



(Ia) (Ib) (II) (III) (IV)

The addition of an excess of alkali to a solution of quinazoline in dilute aqueous acid has now been found, by ultraviolet spectroscopy involving the use of a rapid-flow technique, to give a substance presumed to be covalently hydrated quinazoline (II; X = OH, R = H). However, this substance is very rapidly transformed into quinazoline, its half-life at pH 10 being about 9 seconds, and could not be isolated. On the other hand, the product [4-6] of addition of alkali to 3-methylquinazolinium iodide was isolated and gave the elemental analysis $C_9H_{10}N_2O$. It could be 3,4-dihydro-4-hydroxy-3-methylquinazoline (II; X = OH, R = Me) (as previously suggested [5,6]) or the ring scission product (IV; R = Me) derived from it by intramolecular amino-group elimination.

The infrared spectrum of this compound, both in the solid state (potassium bromide disc) and in solution in chloroform, showed a strong band at 1621 cm.$^{-1}$ (with a twin peak at 1607 cm.$^{-1}$) but none in the range 1625—1750 cm.$^{-1}$ (whereas the carbonyl stretching band for *o*-aminobenzaldehyde occurs at 1665 cm.$^{-1}$); thus, no carbonyl group is present. Furthermore, the chloroform solution shows a band at 3570 cm.$^{-1}$ ($\varepsilon$ 19) attributable to unassociated O–H but not to N–H stretching (the main band in this region, at 3190 cm.$^{-1}$ in chloroform and at 3100 cm.$^{-1}$ in the solid state, is due to strongly associated molecules). The compound thus has the structure (II; X = OH, R = Me) and not (IV; R = Me).

The ultraviolet absorption spectrum of 3,4-dihydro-4-hydroxy-3-methylquinazoline (see Table 1) is the same in water and in cyclohexane (apart from a solvent shift of 4 m$\mu$), showing that no complication occurs in aqueous solution. A comparison with the ultraviolet spectrum of 3,4-dihydro-3-methylquinazoline [3] shows that the replacement of $H_{(4)}$ in (II; X = H, R = Me) by OH causes a (very surprising) hypsochromic shift of the

* Part II, *J.*, 1961, 2697.

[1] Albert, *Chem. Soc. Special Publ.* No. 3, 1955, p. 138.
[2] Osborn, Schofield, and Short, *J.*, 1956, 4191.
[3] Albert, Armarego, and Spinner, *J.*, 1961, 2689.
[4] Gabriel and Colman, *Ber.*, 1904, **37**, 3643.
[5] Schöpf and Oechler, *Annalen*, 1936, **523**, 1.
[6] Fry, Kendall, and Morgan, *J.*, 1960, 5062.

XUM

band near 300 mμ by 28 mμ. A comparison of the ultraviolet spectrum of the short-lived abnormal neutral species of quinazoline with that of 3,4-dihydroquinazoline shows a similar shift of 26 mμ, which strongly suggests that the former is substance (II; X = OH, R = H); in agreement with this, it has a p$K_a$ value of 7·77, which is similar to 7·64 obtained for (II; X = OH, R = Me).

A comparison of the ultraviolet spectra of the abnormal quinazoline cation and the (also abnormal) 3-methylquinazolinium ion (see Table 1) with those of the ions (I; X = R = H) [3] and (I; X = H, R = Me) reveals hypsochromic shifts of 20 and 18 mμ, respectively, but, in view of the large spectral shifts observed on replacing X = H by X = OH in the above neutral molecules, these represent evidence for, rather than against, the structures (I; X = OH, R = H) and (I; X = OH, R = Me) for the two abnormal ions. Two further pieces of evidence against the alternative structures (III) have now been obtained.

First, on addition of a concentrated aqueous solution of quinazoline to benzidine in glacial acetic acid, the red colour characteristic of aromatic aldehydes [7] is not obtained in the cold. Secondly, the ultraviolet spectrum of quinazoline in 1·2N-hydrogen chloride in anhydrous methanol is identical with that of quinazoline in aqueous acid at pH 1, although in anhydrous methanol no cation analogous to (III) should be obtainable; however, the spectrum of the ion (I; X = OMe) should closely resemble that of the ion (I; X = OH). Further, 3-methylquinazolinium iodide " methanolate " (which, in the solid state, is known to retain the elements of $CH_3{\cdot}OH$ very tenaciously [4,5]) has the same

TABLE 1.

Ultraviolet spectra.

| Compound | Solvent | pH (or $H_0$) | Species [a] | $\lambda_{max.}$ (mμ) (inflexions in italics) | log ε |
|---|---|---|---|---|---|
| 3,4-Dihydro-3-methylquinazoline [b] | $H_2O$ | 11·5 | N | *219* + 225 + 231; 304 | *3·99* + 4·01 + 4·04; 3·90 |
| | $H_2O$ | 7·0 | C | 214 + 218 + *224*; 284 | 4·23 + 4·24 + *4·04*; 3·79 |
| 3,4-Dihydro-4-hydroxy-3-methylquinazoline [c] | $H_2O$ | 10·0 | N | <210 + *218* + *225*; 276 | >4·30 + *3·99* + *3·85*; 4·06 |
| | $H_2O$ | 2·0 | AC | <207; 266 | >4·38; 3·98 |
| *o*-Toluidine [d] | n-$C_6H_{14}$ | | N | 234; 285 | 3·93; 3·32 |
| *o*-Aminobenzyl alcohol | n-$C_6H_{14}$ | | N | 240; 290 | 3·80; 3·36 |
| 3,4-Dihydroquinazoline [b] | $H_2O$ | 11·5 | N | *217* + 221 + *227*; 291 | *4·07* + 4·09 + *3·97*; 3·76 |
| | | 7·0 | C | 212 + 217 + *225*; 280 | 4·26 + 4·25 + *4·01*; 3·69 |
| 3,4-Dihydro-4-methylquinazoline [e] | $H_2O$ | 11·5 | N | 221 + *226*; 287 | 4·12 + *4·00*; 3·80 |
| | | 7·0 | C | 212 + 216 + *223*; 277 | 4·24 + 4·23 + *3·99*; 3·70 |
| 3,4-Dihydroquinazolinium-4-sulphonate [f] | $H_2O$ | 4·0 | Z [b] | 222 + *229*; 282 | 4·17 + *3·93*; 3·66 |
| | $H_2O$–HCl | −3·4 | C | <212 + *217* + *222*; 279 | >4·30 + *4·54* + *4·43*; 3·73 |
| 4-Cyano-3,4-dihydroquinazoline [f] | $H_2O$ | 1·0 | C | 210 + 216 + *222*; 275 | 4·35 + 4·29 + *4·11*; 3·80 |
| Quinazoline | $H_2O$ | 1·0 | AC [b] | 208; 260 | 4·20; 3·91 |
| | $H_2O$ | 9·8 | AN [g] | 265 | 3·97 |

[a] N = neutral molecule; AN = abnormal (short-lived) neutral molecule; C = (normal) cation; AC = abnormal cation; Z = zwitterion (I; R = H, X = $SO_3^-$). [b] Ref. 3. [c] p$K_a$ value, 7·64 ± 0·03. [d] Wolf and Herold, *Z. phys. Chem.*, 1931, *B*, **13**, 201; Dede and Rosenberg, *Ber.*, 1934, **67**, 147. [e] p$K_a$ value, 9·19 ± 0·04. [f] p$K_a$ value for proton addition not known. [g] p$K_a$ value, 7·77; this substance was kindly examined by Dr. D. D. Perrin.

ultraviolet spectrum [3] as 3-methylquinazolinium iodide " hydrate," but paper chromatography in aqueous solution showed the " hydrate " to be different from the " methanolate," at pH 5 and at pH 11. The " methanolate " cation must have the structure (I; X = OMe, R = Me) and the corresponding neutral molecule (the *pseudo*-base) the structure (II;

[7] Feigl, " Spot Tests in Organic Analysis," Elsevier, Amsterdam, 1956, p. 210.

X = OMe, R = Me) (and any replacement of OMe by OH in aqueous medium must be slow in the neutral molecule and very slow in the cation).

*The Effect of 4-Substituents on the Ultraviolet Spectrum of 3,4-Dihydroquinazoline.*—The hypsochromic shift of 20—25 mμ produced by the replacement of the hydrogen atom by hydroxyl in the (non-conjugating) 4-position in molecules (II) and (I) is very remarkable and contrary to previous experience. Thus, the replacement of α-hydrogen by hydroxyl causes a bathochromic shift of the spectrum by about 5 mμ in *o*-toluidine (see Table 1), and shifts of +5·5 mμ (*K*-band, at 236 mμ) and −2 mμ (*B*-band, at 291 mμ) in *p*-toluidine,[8] of +3 mμ (*K*-band) and −4 mμ (*B*-band) in *p*-anisidine,[9] and of −2·5 mμ (*K*-band) in *p*-nitrotoluene;[8] the shift due to hydroxyl in such a position (*i.e.*, at a saturated carbon atom attached to a conjugated system) is normally smaller [8,9] than that caused by more strongly electron-withdrawing groups (such as cyano).

In the ions (I; R = H), by contrast, the replacement of X = H by other groups usually produces only small and irregular displacements of the band at 280 mμ (see Table 1), *viz.*, X = $SO_3^-$, +2 mμ; X = $SO_3H$, −1 mμ; X = $CH_3$, −3 mμ; X = CN, −5 mμ; as compared with X = OH, −20 mμ. For the molecules (II; R = H) the figures are X = Me, −4 mμ and X = OH, −26 mμ. (When X = CN or $SO_3^-$ elimination of HCN or $HSO_3^-$ is very rapid, and no spectra could be obtained.) No satisfactory explanation for the large spectral shift produced by X = OH is available.

## Experimental

Analyses were by Dr. J. E. Fildes and her staff.

*Physical Measurements.*—Ionisation constants and spectra were determined as before.[3] The rapid-flow measurements [10] were carried out by means of a modified Chance apparatus from which the rapidly-mixed liquid was passed into a spectrophotometric cell inserted in a Perkin–Elmer Spectracord instrument.

*Materials.*—2-Aminobenzyl alcohol [11] and 4-cyano-3,4-dihydroquinazoline [12] were prepared as described in the literature.

*3,4-Dihydro-4-hydroxy-3-methylquinazoline.*—Anhydrous 3-methylquinazolinium iodide prepared [6] from 2·2 g. of resublimed quinazoline and 1·7 ml. of methyl iodide) in water (15 ml.) was treated, with cooling, with 33% aqueous potassium hydroxide (3·0 ml.). After a few minutes the *pseudo*-base that had crystallised in needles was filtered off, washed with water until the filtrate was no longer alkaline, and dried at 100° to constant weight (1·91 g., 70%). (This product could not be isolated from the action of alkali on the methanolate [4,5] of 3-methylquinazolinium iodide.) It decomposes slowly in boiling water or benzene, and is best purified by adding boiling water to the finely powdered material, filtering immediately, and quickly chilling the filtrate to initiate crystallisation. Purified in this manner it had m. p. 167—168° (Gabriel and Colman,[4] and Schöpf and Oechler,[5] gave 162—163°; Fry, Kendall, and Morgan [6] 164—165°) (Found: C, 66·8; H, 6·0; N, 17·25. Calc. for $C_9H_{10}N_2O$: C, 66·7; H, 6·2; N, 17·3%).

These compounds have been proved to be the 3- and not the 1-methylated derivatives,[5,6] and in the present work they were obtained in a chromatographically pure state. At pH 5 (3% aqueous ammonium chloride, 20 hr. at 5°) the methanolate gave only one spot, with $R_F$ 0·89, and the *pseudo*-base one with $R_F$ 0·79 (ascending method).

*3,4-Dihydro-4-methylquinazoline.*—3,4-Dihydro-4-methylquinazoline picrate [12] (prepared by the action of methylmagnesium iodide on quinazoline, followed by treatment with ethanolic picric acid) [4·8 g.; m. p. 234—236° (decomp.)], suspended in chloroform, was shaken with 5N-aqueous sodium hydroxide, and the aqueous layer was diluted with water until all the sodium picrate had dissolved. The chloroform layer was washed with 10N-aqueous sodium hydroxide and dried ($K_2CO_3$). The chloroform was removed at 30°/15 mm., and the residue

[8] Burawoy and Spinner, *J.*, 1955, 2557.
[9] Spinner, *Spectrochim. Acta*, 1961, **17**, 545.
[10] Perrin, *J.*, in the press.
[11] Nystrom and Brown, *J. Amer. Chem. Soc.*, 1947, **69**, 2548.
[12] Higashino, *J. Pharm. Soc. Japan*, 1960, **80**, 5062.

distilled (b. p. 124°/2·5 mm.). The pale yellow viscous distillate (1·3 g., 70%) crystallised and had m. p. 78—79° (Found: C, 73·8; H, 7·0; N, 18·8. $C_9H_{10}N_2$ requires C, 73·9; H, 6·9; N, 19·2%).

The correctness of the assigned structure was proved by oxidation, with potassium ferricyanide, to 4-methylquinazoline, which was isolated as the picrate, m. p. and mixed m. p. 180—181°.

We are greatly indebted to Dr. D. D. Perrin, who demonstrated the existence of the short-lived abnormal (hydrated) species of neutral quinazoline and measured its physical properties. We also thank Mr. D. T. Light for technical assistance.

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## 1043. *Essential Fatty Acids. Part II.*[1] *Synthesis of (±)-Vernolic, Linoleic, and γ-Linolenic Acid.*

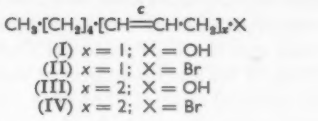
By J. M. Osbond.

The first synthesis of a naturally occurring unsaturated epoxy-acid, vernolic acid (X), is described. 1-Bromo-oct-*cis*-2-ene (II), and the di-Grignard complex of dec-9-ynoic acid gave octadeca-*cis*-12-en-9-ynoic acid (V). Partial reduction then gave linoleic acid (XII); epoxidation of the acid (V) followed by stereoselective reduction of the acetylenic bond gave (±)-vernolic acid (X). Similarly 1-bromoundeca-2,5-diene (IV) and hept-6-ynoic acid gave the $C_{18}$-dienynoic acid (VII) which on partial reduction furnished γ-linolenic acid (XIII).

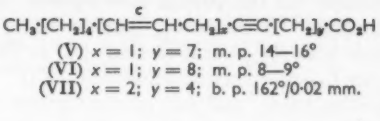
The principal seed-oil acid from *Vernonia anthelmintica*,[2] vernolic acid, is an epoxy-acid that until recently was unique. The structure of vernolic acid was determined by Gunstone and his co-workers[2,3] as *cis*-12,13-epoxyoctadec-*cis*-9-enoic acid (X) and the acid was later obtained crystalline by Smith, Koch, and Wolff[4] and by Chisholm and Hopkins.[5] *V. anthelmintica* is an Indian plant with alleged medicinal value (cf. Gunstone[1] for leading references; in particular, Majumdar[6] found the seed oil effective against round-worms). Other members of this group have now been isolated from various seed oils, namely, *cis*-15,16-epoxylinoleic acid,[7] *cis*-9,10-epoxyoctadec-*cis*-12-enoic acid[8] and *cis*-9,10-epoxystearic acid.[9] None of these unsaturated epoxy-acids has so far been synthesised. In Part I,[1] 1,4-diacetylenic and *cis*-1,4-dienoic acids ("skipped unsaturation") were synthesised by addition of a propargyl halide to the di-Grignard complex of an ω-acetylenic acid followed by partial reduction. This route allowed a synthesis of vernolic acid to be made.[10] The synthesis depends on the greater rate of epoxidation of ethylenic than of acetylenic bonds,[11] and the selective stereospecific partial reduction of an acetylenic bond without the opening of a neighbouring epoxide ring.

Oct-*cis*-2-en-1-ol (I), containing only traces of the *trans*-isomer, was prepared from

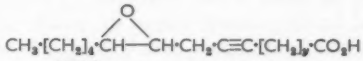
[1] Part I, Osbond, Philpott, and Wickens, *J.*, 1961, 2779.
[2] Gunstone, *J.*, 1954, 1611.
[3] Bharucha and Gunstone, *J.*, 1956, 1611.
[4] Smith, Koch, and Wolff, *J. Amer. Oil Chemists' Soc.*, 1959, **36**, 219.
[5] Chisholm and Hopkins, *Chem. and Ind.*, 1960, 1134.
[6] Majumdar, *Indian J. Pharmacol.*, 1943, **5**, 61.
[7] Gunstone and Morris, *J.*, 1959, 2127.
[8] Smith, Bagby, Lohmar, Glass, and Wolff, *J. Org. Chem.*, 1960, **25**, 218.
[9] Chisholm and Hopkins, *Chem. and Ind.*, 1959, 1154.
[10] Osbond, *Proc. Chem. Soc.*, 1960, 221.
[11] Cf. Raphael, "Acetylenic Compounds in Organic Chemistry," Butterworths Scientific Publ., London, 1955, p. 33.



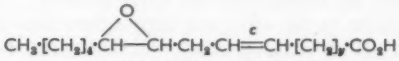
(I) $x = 1$; X = OH
(II) $x = 1$; X = Br
(III) $x = 2$; X = OH
(IV) $x = 2$; X = Br



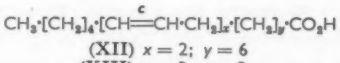
(V) $x = 1$; $y = 7$; m. p. 14—16°
(VI) $x = 1$; $y = 8$; m. p. 8—9°
(VII) $x = 2$; $y = 4$; b. p. 162°/0·02 mm.



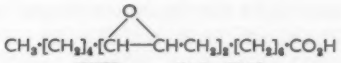
(VIII) $y = 7$; m. p. 55—57°
(IX) $y = 8$; m. p. 52·5—54·5°



(X) $y = 7$; m. p. 35—36°
(XI) $y = 8$; m. p. 40—41°



(XII) $x = 2$; $y = 6$
(XIII) $x = 3$; $y = 3$



(XIV) m. p. 76·5—77·5°

oct-2-yn-1-ol by partial reduction with Lindlar's catalyst.[12] Its reaction with phosphorus tribromide and pyridine was carried out under a variety of conditions; in nearly all cases the proportion of the *trans*-bromide (cf. II) formed was high as shown by the infrared band at $\nu_{max.}$ 965 cm.$^{-1}$; the bands at 1657 (*trans*-C=C) and 1645 cm.$^{-1}$ (*cis*-C=C) were also found to be useful (see Experimental section). Conditions for avoiding this not unexpected easy stereomutation were found and essentially pure *cis*-bromide (II) was then obtained in high yield. The avoidance of pyridine and light was important. Similarly partial reduction of undeca-2,5-diyne-1-ol [1] gavè undeca-*cis*-2,5-diene-1-ol (III) with only a trace of *trans*-isomer; reaction with phosphorus tribromide under similar conditions gave 1-bromoundeca-*cis*-2,5-diene (IV) although in this case some *trans*-isomer was invariably formed.

The di-Grignard reagent from dec-9-ynoic acid in tetrahydrofuran and the bromide (II) were condensed in the presence of cuprous cyanide,[1] to give crystalline octadec-*cis*-12-en-9-ynoic acid (V) in 64% yield; the infrared spectrum showed only a trace of *trans*-isomer. The linearity of the acid was confirmed by reduction over Adams catalyst to pure stearic acid in 90% yield after an uptake of 6·35 equiv. of hydrogen. Similarly the di-Grignard derivative of undec-10-ynoic acid with the bromide (II), and hept-6-ynoic acid with 1-bromoundeca-*cis*-2,5-diene (IV), gave nonadeca-*cis*-13-en-10-ynoic acid (VI) and octadeca-*cis*-9,10-dien-6-ynoic acid (VII), respectively; in the spectrum of the latter acid a distinct *trans*-band was noted at 965 cm.$^{-1}$.

Partial reduction of the $C_{18}$-enynoic (V) and the $C_{18}$-dienynoic acids (VII) with Lindlar catalyst in light petroleum furnished a new route to linoleic (XII) and γ-linolenic acid (XIII), both previously synthesised from polyacetylenic acids.[1,13] The crude acids were characterised by formation of the known crystalline 9,10,12,13-tetrabromo- and 6,7,9,10,12,13-hexabromo-stearic acid, respectively.

Treatment of the $C_{18}$-*cis*-enynoic acid (V) with peracetic acid in glacial acetic acid gave, after 75% of the peracetic acid had been consumed (4 hr.), a crystalline epoxide (VIII) in 52% yield; similarly the $C_{19}$-enynoic acid (VI) gave the crystalline epoxide (IX). In both cases the presence and nature of the oxygen atom was shown by analysis (the oxiran oxygen was determined by the direct titration method of Durbetaki [14]) and by the infrared spectra (*cis*-epoxide bands [15] at 775 and 810 cm.$^{-1}$; no *cis*-ethylenic bands at 3040 and 1650 cm.$^{-1}$). The final step was effected with Lindlar's catalyst, which was found to be

[12] Lindlar, *Helv. Chim. Acta*, 1952, **35**, 446.
[13] Raphael and Sondheimer, *J.*, 1950, 2100; Gensler and Thomas, *J. Amer. Chem. Soc.*, 1951, **73**, 4601; Walborsky, Davis, and Howton, *ibid.*, p. 2590.
[14] Durbetaki, *Analyt. Chem.*, 1956, **28**, 2000.
[15] Cf. Shreve, Heether, Knight, and Swern, *Analyt. Chem.*, 1951, **23**, 277; Patterson, *ibid.*, 1954, **26**, 823.

very suitable for the partial stereospecific reduction of the acetylenic bond to the *cis*-ethylenic bond. Thus the $C_{18}$-epoxide (VIII) gave the crystalline *cis*-12,13-epoxyoctadeca-*cis*-9-enoic acid [(±)-vernolic acid] (X) in 70% yield and the $C_{19}$-epoxide (IX) gave the crystalline $C_{19}$-*cis*-epoxy-*cis*-enoic acid (XI). Analysis of both acids indicated one double bond (iodine value) and one oxiran oxygen;[14] the infrared spectra showed a *cis*-double bond (no *trans*-band and a *cis*-epoxide). The melting point of our synthetic (±)-vernolic acid (m. p. 35—36°) was higher than that recorded for the natural isomer (m. p. 25—28°;[3] 30—31°[4]) or the partially synthetic material obtained from linoleic acid[16] (m. p. 18—19°). To prove the structure (X) for our product two transformations were carried out. Following Bharucha and Gunstone[3] we converted the epoxide (X) by acetic acid into (±)-*threo*-12,13-dihydroxyocta-9-enoic acid, which on reduction gave (±)-*threo*-12,13-dihydroxystearic acid, both having correct m. p.s. Secondly, the epoxide (X) with one equivalent of peracetic acid gave *cis*-9,10,12,13-diepoxystearic acid (XIV), m. p. 76·5—77·5°; the diepoxide derived from linoleic acid was then prepared[17] (m. p. 78°) and found to be identical with the totally synthetic material (XIV) by mixed melting point and infrared spectral comparison.

## Experimental

The infrared spectra were determined by Dr. A. Wagland for liquid films or, for solids, Nujol suspensions, unless otherwise stated.

*Oct*-cis-2-*en*-1-*ol* (I).—Oct-2-yn-1-ol (100·9 g., 0·8 mole) in purified light petroleum (b. p. 69—77°; 2 l.) containing quinoline (1 c.c.) was hydrogenated with Lindlar catalyst[12] (12·0 g.) at 20°/1 atm. with stirring. The uptake of hydrogen (19·7 l.; theor., 19·24 l.) was complete in 4·5 hr. and then stopped completely. The solution was filtered, washed with 2N-hydrochloric acid and water, and dried ($Na_2SO_4$). The distilled product had b. p. 98—102°/10—15 mm., $n_D^{21}$ 1·4472 (97·0 g., 98%). The infrared spectrum showed only a trace of *trans*-double bond at 965 cm.$^{-1}$. (Colonge and Poilane[18] give b. p. 88°/11 mm., $n_D^{20}$ 1·4470.)

1-*Bromo-oct*-cis-2-*ene* (II).—Oct-*cis*-2-en-1-ol (38·5 g.; 0·3 mole) in dry ether (400 c.c.) was treated with phosphorus tribromide (29·8 g., 10·2 c.c.) during 0·5 hr.; the solution was stirred and protected from light. The solution was refluxed for 2·5 hr., cooled, poured on ice-water, shaken, and extracted 3 times with ether. The extracts were combined, washed with saturated sodium hydrogen carbonate solution and water (twice), and dried ($Na_2SO_4$). The ether was removed and the bromide (55 g., 96%) was used directly; this material contained very little *trans*-isomer (band at 965 cm.$^{-1}$) but each batch should be checked for this impurity. The amount of *cis*-isomer is difficult to estimate; however, two peaks occur at 1657 and 1645 cm.$^{-1}$, the former is associated with *trans*-, the latter with *cis*-double bonds (C=C stretching bonds[19]). In good samples (mostly *cis*) only one peak at 1645 cm.$^{-1}$ was observed and *vice versa*. The *bromide* (45·9 g.) has b. p. 104—106°/35 mm., $n_D^{20}$ 1·4762, but distillation slightly increases the amount of *trans*-isomer (Found: C, 50·4; H, 7·9; Br, 41·45%; I val., 133. $C_8H_{15}Br$ requires C, 50·3; H, 7·9; Br, 41·8%; I val., 132).

*Undeca*-cis-2,5-*dien*-1-*ol* (III).—Undeca-2,5-diyne-1-ol[1] (17·9 g.) in purified light petroleum (b. p. 60—80°; 300 c.c.) was reduced with Lindlar catalyst (4 g.) in the presence of 5% quinoline–light petroleum solution (5 c.c.). The uptake of hydrogen stopped at 4850 c.c. (theor., 5150 c.c.). The solution was filtered, washed with 2N-sulphuric acid and water, dried ($Na_2SO_4$), and evaporated. The *alcohol* was distilled (b. p. 100—101°/0·005 mm.) and had $n_D^{20\cdot5}$ 1·4709 (86% yield) (Found: C, 77·9; H, 12·0%; I val., 301·2. $C_{11}H_{20}O$ requires C, 78·5; H, 12·0%; I val., 301·7). The infrared spectrum showed only a small amount of *trans*-double bond; the ultraviolet absorption maximum (in EtOH) was at 229 mμ ($E_{1\,cm.}^{1\%}$ 23·4).

1-*Bromoundeca*-cis-2,5-*diene* (IV).—The alcohol (III) (15·3 g.) in dry ether (200 c.c.) was treated dropwise at 20° with phosphorus tribromide (9·02 g.) during ½ hr. in the dark. The

[18] Pigulevskii and Naidenova, *J. Gen. Chem.* (*U.S.S.R.*), 1958, **28**, 234.
[17] Swern and Dickel, *J. Amer. Chem. Soc.*, 1954, **76**, 1957; Pigulevskii and Kuranova, *Zhur. prikład. Khim.*, 1955, **28**, 1353.
[18] Colonge and Poilane, *Compt. rend.*, 1954, **238**, 1821.
[19] Cf. Cross, "Introduction to Practical Infra-Red Spectroscopy," Butterworths Scientific Publ. London, 1960, p. 58.

solution was refluxed for 2½ hr., cooled, poured on ice-water, and extracted 3 times with ether; the extracts were washed, etc., as above. The *bromide* had b. p. 88—91°/0·005 mm. (18·05 g., 86%), $n_D^{18}$ 1·4929 (Found: C, 57·1; H, 8·3; Br, 34·3. $C_{11}H_{19}Br$ requires C, 57·15; H, 8·25; Br, 34·6%). The infrared spectrum showed some *trans*-isomer to be present.

*Octadeca*-cis-12-*en*-9-*ynoic Acid* (V).—To magnesium (14·6 g., 0·6 g.-atom) under tetrahydrofuran (120 c.c.) was added ethyl bromide (71·9 g., 0·66 mole) in tetrahydrofuran (200 c.c.) dropwise with stirring at 0°. The solution was then stirred at room temperature for 2 hr., cooled to 0°, and treated dropwise with dec-9-ynoic acid [20] (50·4 g., 0·3 mole) in tetrahydrofuran (200 c.c.) in 1½ hr. The whole was then stirred at 20° for 2 hr. Cuprous cyanide (2·0 g.) was added followed by 1-bromo-oct-*cis*-2-ene (57·4 g., 0·3 mole) in tetrahydrofuran (50 c.c.) in 10 min. The mixture became warm and refluxed slightly. After being stirred at 20° overnight under nitrogen the solution was poured on ice and 2N-sulphuric acid and extracted thrice with ether. The ether extracts were shaken with 2N-ammonia; this alkaline extract was acidified with concentrated hydrochloric acid, and extracted with ether, which was then washed with water, dried ($Na_2SO_4$), and distilled, giving unchanged dec-9-ynoic acid (17·1 g.), b. p. 78—160°/0·01—0·005 mm., $n_D^{20}$ 1·4592, and the *enynoic acid* (35·3 g., 64% based on unrecovered decynoic acid), b. p. 166—172°/0·005 mm., $n_D^{20}$ 1·4730. This material was sufficiently pure for the next stage. Crystallisation from light petroleum (b. p. 40—60°) at −20° gave the pure acid as plates, m. p. 14—16°, $n_D^{20}$ 1·4734, transparent to ultraviolet light (the infrared spectrum showed only a trace of *trans*-double bond) (Found: C, 77·4; H, 10·8. $C_{18}H_{30}O_2$ requires C, 77·65; H, 10·9%).

*Nonadeca*-cis-13-*en*-10-*ynoic Acid* (VI).—Similarly the di-Grignard complex of undec-10-ynoic acid (54·7 g., 0·3 mole) was prepared as described above from magnesium (14·6 g.) and ethyl bromide (71·9 g.) in tetrahydrofuran (520 c.c.) at 0°. To this solution was added cuprous cyanide (2·0 g.) and 1-bromo-oct-*cis*-2-ene (57·0 g.) in tetrahydrofuran (50 c.c.) at 20°. The resulting *acid*, b. p. 156—172°/0·06—0·1 mm., $n_D^{21}$ 1·4719 (21·47 g.), was acccompanied by recovered undec-10-ynoic acid (18·2 g.). Crystallisation from light petroleum at −30° gave the pure acid, m. p. 8—9° (trace of *trans*-double bond) (Found: C, 77·6; H, 11·1. $C_{19}H_{32}O_2$ requires C, 78·0; H, 11·0%), having no ultraviolet absorption above 220 mμ.

*Octadeca*-cis-9,12-*dien*-6-*ynoic Acid* (VII).—Similarly ethyl bromide (25·1 g.) in tetrahydrofuran (25 c.c.) was added to magnesium (4·9 g.) under tetrahydrofuran (25 c.c.) at 0° during ½ hr. After a further ½ hr. at 20° hept-6-ynoic acid (12·6 g.) in tetrahydrofuran (25 c.c.) was added dropwise at 0° (ice–salt cooling) in ½ hr. A further 50 c.c. of tetrahydrofuran was then added and the mixture stirred at 20° for 2 hr., then cuprous cyanide (0·5 g.) was added. 1-Bromo-undeca-*cis*-2,5-diene (11·6 g.) in tetrahydrofuran (25 c.c.) was added at 20° in ½ hr. under nitrogen and the mixture stirred for 16 hr. The *acid*, isolated in the usual way, had b. p. 162—164°/0·0025 mm., $n_D^{18\cdot5}$ 1·4830 (9·8 g., 70%) (Found: C, 78·45; H, 10·0. $C_{18}H_{26}O_2$ requires C, 78·2; H, 10·2%). A band at 965 cm.$^{-1}$ showed some *trans*-isomer to be present.

*Stearic Acid*.—Octadeca-*cis*-12-en-9-ynoic acid (2·62 g.) in methanol (25 c.c.) containing prereduced Adams catalyst (0·1 g.) was reduced at 20°/1 atm. Absorption (750 c.c.; theor., 709 c.c.) was rapid (20 min.) and the resulting acid crystallised. The solution was warmed, filtered, and cooled to 0°. Stearic acid separated as plates (2·40 g., 90%), m. p. 69·5—70°. A mixed m. p. with an authentic sample was 68—70°.

*Octadeca*-cis-9,12-*dienoic Acid* (*Linoleic Acid*) (XII).—Octadeca-*cis*-12-en-9-ynoic acid (V) (5·27 g.) in light petroleum (b. p. 67—70°; 130 c.c.) and a 5% solution of quinoline in light petroleum (3 c.c.) was hydrogenated at 20°/1 atm. with Lindlar's catalyst (1·0 g.). After absorption of one mol. of hydrogen (458 c.c.; theor., 483 c.c.) there was a sharp break in the hydrogenation curve and the reaction was stopped. The filtered solution was treated with bromine dropwise at 0° with stirring until a red colour persisted. The solid was filtered off, washed with light petroleum, and dried. The 9,10,12,13-tetrabromostearic acid (3·8 g.), crystallised from methylene chloride, had m. p. 114—115·5° (Found: C, 36·0; H, 5·3; Br, 53·4. Calc. for $C_{18}H_{32}Br_4O_2$: C, 36·2; H, 5·4; Br, 53·3%). A mixed m. p. with a specimen (m. p. 115—116°) prepared from poppy-seed oil [21] gave no depression. A comparison of their infrared spectra showed no differences.

*Octadeca*-cis-6,9,12-*trienoic Acid* (*γ-Linolenic Acid*) (XIII).—Similarly the dienynoic acid (VII) (4·06 g.) in light petroleum (b. p. 60—80°; 60 c.c.) with 5% quinoline–light petroleum

[20] Black and Weedon, *J.*, 1953, 1785; Crombie and Jacklin, *J.*, 1957, 1622.
[21] McCutcheon, *Org. Synth.*, 1942, **22**, 75.

XUM

(2 c.c.) and Lindlar catalyst (1·2 g.) (uptake, 355 c.c.; theor., 355 c.c.) gave γ-linolenic acid that was treated in ether with bromine at 0°. The insoluble 6,7,9,10,12,13-hexabromostearic acid (1·10 g.), when crystallised from ethyl methyl ketone, had m. p. 201·5—202° alone or mixed with a previous specimen [1,22] (Found: C, 28·8; H, 3·9; Br, 62·7. Calc. for $C_{18}H_{30}Br_6O_2$: C, 28·5; H, 4·0; Br, 63·3%).

*Octadeca*-cis-12,13-*epoxy*-9-*ynoic Acid* (XIII).—Octadeca-*cis*-12-en-9-ynoic acid (V) (30·0 g.) was treated at 5° with an 8·36% solution of peracetic acid in glacial acetic acid (107·8 c.c., 1·1 moles). The solution was kept at 5° for 1 hr. and at 20° for 3 hr., then poured on ice-water. In a preliminary experiment portions were withdrawn at intervals and the peracetic acid content determined by titration: after 4 hr. *ca.* 75% had been consumed and little more reacted after this time. The sticky white solid (31·2 g.) was filtered off, washed with water, dried, and crystallised from light petroleum (b. p. 40—60°; 150 c.c.) at 0°, giving the *epoxide* (16·4 g., 52%), m. p. 52·5—55°. Recrystallisation from light petroleum gave a sample, m. p. 55—57° (Found: C, 73·1; H, 10·2; O, 16·8; oxiran-O, 5·2. $C_{18}H_{30}O_2$ requires C, 73·4; H, 10·3; O, 16·3; oxiran-O, 5·4%), $\nu_{max.}$ (in $CS_2$) 810 (*cis*-epoxide), 775 and 1000 cm.$^{-1}$.

*Nonadeca*-cis-13,14-*epoxy*-10-*ynoic Acid* (IX).—Similarly, nonadeca-*cis*-13-en-10-ynoic acid (VI) (21·5 g.) gave a crude product (25·8 g.) that, crystallised from light petroleum (b. p. 40—60°; 100 c.c.), afforded the crude epoxide (12·23 g.), m. p. 46—48°. Several crystallisations from light petroleum or methanol gave the *epoxide* (3·9 g.) as needles, m. p. 52·5—54·5° (Found: C, 73·7; H, 10·4. $C_{19}H_{32}O_2$ requires C, 74·0; H, 10·5%). This had no infrared band at 3040 or 1650 cm.$^{-1}$ (*cis*-double bond), but an epoxide band at 810 cm.$^{-1}$ and an additional band at 775 cm.$^{-1}$.

*Octadeca*-cis-12,13-*epoxy*-cis-9-*enoic Acid* (X) [(±)-*Vernolic Acid*].—The epoxy-acetylenic acid (VIII) (5·88 g.) in purified light petroleum (b. p. 67—77°; 200 c.c.) and a 5% quinoline–light petroleum solution (8 c.c.) was hydrogenated with Lindlar catalyst (2·0 g.) at 20°/1 atm. (uptake, 496 c.c.; 1 mol., 491 c.c.). The solution was filtered, concentrated to *ca.* 50 c.c., and cooled in ice–salt. The colourless prisms (4·17 g., 70%), m. p. 32·5—35°, were collected and recrystallised from light petroleum (b. p. 40—60°) at −10°. The pure epoxy-acid had m. p. 35—36°. Natural vernolic acid is recorded as being liquid at room temperature with $[\alpha]_D$ −8°,[2] and as having m. p. 25—28° [4] and 30—31°.[5] The partially synthetic (±)-form had m. p. 18—19° [16] (Found: C, 72·6; H, 10·8; O, 15·9; oxiran-O, 5·4%; I val., 93, 94. Calc. for $C_{18}H_{32}O_3$: C, 72·9; H, 10·9; O, 16·2; oxiran-O, 5·4%; I val., 85·6). The infrared spectrum (in $CS_2$) showed bands at 820 (*cis*-epoxide), 775, and 1105 cm.$^{-1}$. A double bond was shown at 720, 1650, and 3040 cm.$^{-1}$; there was no *trans*-isomer band at 965 cm.$^{-1}$.

cis-13,14-*Epoxynonadeca*-cis-10-*enoic Acid* (XI).—Similarly the epoxy-acetylenic acid (IX) (3·08 g.) gave an epoxy-enoic *acid* (XI) that crystallised from light petroleum (b. p. 40—60°) as prisms, m. p. 40—41° (also m. p. 35·5—36·5°; the infrared spectra of the two samples were identical) (Found: C, 74·1; H, 11·3; O, 15·1%; I val., 82. $C_{19}H_{34}O_3$ requires C, 73·5; H, 11·0; O, 15·5%; I val., 81·75), $\nu_{max.}$ 815 (epoxide), 715 (cis C=C), and 2980 cm.$^{-1}$ (no *trans*-double bond).

(±)-threo-12,13-*Dihydroxyoctadec*-9-*enoic Acid*.—*cis*-12,13-Epoxyoctadeca-*cis*-9-enoic acid (1·84 g.) in glacial acetic acid (50 c.c.) was heated at 95° for 9 hr. The acetic acid was removed under reduced pressure and the resulting syrup boiled with potassium hydroxide (5 g.) in water (20 c.c.) and methanol (80 c.c.) for 2 hr. The methanol was removed and the solution made acid with 2N-hydrochloric acid and extracted twice with ether. The extracts were washed with water and dried ($Na_2SO_4$). The acid separated from ethyl acetate–light petroleum (b. p. 40—60°) at −40° as prisms (0·9 g.), m. p. 45—48°, and recrystallisation gave the pure acid, m. p. 52—53° [lit.,[2,3] m. p. for the (−)-form, 53—54°, 52—55°; (±)-form [5] 52·5—53°) (Found: C, 69·1; H, 10·9%; I val., 82, 83. Calc. for $C_{18}H_{34}O_4$: C, 68·7; H, 10·9%; I val., 80·7).

(±)-threo-12,13-*Dihydroxystearic Acid*.—The above dihydroxy-acid (0·26 g.) in ethyl acetate (20 c.c.) was hydrogenated with prereduced Adams catalyst (0·05 g.) at 20°/1 atm. (uptake, 21 c.c.; theor., 20·5 c.c.). The filtered, concentrated solution deposited crystals (0·13 g.), m. p. 96—97° [lit.,[22] for (±)-form, m. p. 98·5(?)—97°; the (+)-form [3,5] m. p. 95—96°, 96·5—97°] (Found: C, 68·6; H, 11·5. Calc. for $C_{18}H_{36}O_4$: C, 68·3; H, 11·5%).

cis-9,10,12,13-*Diepoxystearic Acid* (XIV).—(*a*) (±)-Vernolic acid (X) (0·89 g.) was treated with a 9·45% solution of peracetic acid in glacial acetic acid (2·6 c.c.) at 20° for 4 hr., then poured on ice-water. The product (0·88 g.; m. p. 58—68°) was filtered off, washed with water, dried,

[22] Nevenzel and Howton, *J. Org. Chem.*, 1958, **23**, 933.
[23] Huber, *J. Amer. Chem. Soc.*, 1951, **73**, 2730.

and recrystallised thrice from ethanol, to give the diepoxystearic acid, m. p. and mixed m. p. 76·5—77·5° (Found: C, 68·75; H, 10·2; O, 20·6. Calc. for $C_{18}H_{32}O_4$: C, 69·2; H, 10·3; O, 20·5%), $\nu_{max.}$ (in $CS_2$) 815 cm.$^{-1}$ (shoulder at 830) (*cis*-epoxide), identical with that of the specimen recorded below.

(*b*) Linoleic acid (5·35 g.), treated as above, gave the diepoxy-acid, m. p. 78° (lit.,[17] m. p. 77·8—78·2°, 78°) (Found: C, 69·4; H, 10·1; oxiran-O, 9·5. Calc. for $C_{18}H_{32}O_4$: C, 69·2; H, 10·3; oxiran-O, 10·2%).

I thank Mr. B. Gregson-Allcott for skilled assistance.

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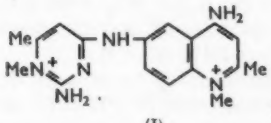
## 1044. *Bisquaternary Salts Related to Quinapyramine (Antrycide). Replacement of the Quinoline Nucleus by Other Heterocycles.*

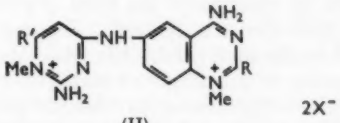
By S. S. BERG and E. W. PARNELL.

Some analogues of quinapyramine [4-amino-6-(2-amino-4-methylpyrimid-6-ylamino)quinaldine 1,3′-bismethochloride] are described in which the quinaldine residue has been replaced by the bicyclic heterocyclic systems, quinazoline, phthalazine, indazole, benzothiazole, benzoxazole, benzisoxazole, and benzimidazole. Some of the compounds showed trypanocidal activity.

THE trypanocidal activity of quinapyramine [1] (Antrycide) (I) led us to examine the effect on activity of replacing the quinaldine residue by quinazoline. The compounds (II; R′ = R″ = H or Me) obtained had similar activity to that of quinapyramine against *Trypanosoma congolense* and *T. rhodesiense*.* This suggested that the activity of these compounds might be a function of the pyrimidine portion and so some analogues of quinapyramine containing other bicyclic heterocyclic nuclei were prepared. Only those from phthalazine and benzoxazole showed significant activity, the former being comparable with quinapyramine.




(I)




(II)

Two general preparative routes were employed: (*a*) reaction of 2-amino-4-chloro-6-methylpyrimidine (III) with the appropriate heterocyclic diamine, with subsequent quaternisation; and (*b*) direct reaction of the methiodide of the pyrimidine (III) with the quaternary salt of the heterocyclic diamine.

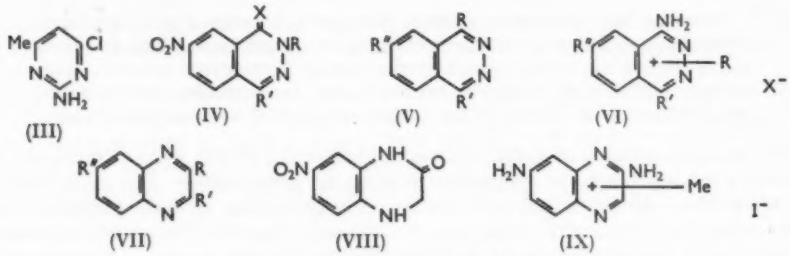
4,6-Diamino-2-methylquinazoline was prepared by reduction of 4-amino-2-methyl-6-nitroquinazoline [3] and was allowed to react with the chloro-compound (III). Treatment of the product with methyl toluene-*p*-sulphonate and subsequent conversion into the dichloride gave a product (II; R′ = R″ = Me, X = Cl) identical with that obtained from the methiodide of the pyrimidine (III) with 4,6-diamino-1,2-dimethylquinazolinium chloride [3] in hydrochloric acid.

Direct bromination of 6-nitrophthalide by recorded methods [4,5] was unsatisfactory for

* These compounds were claimed to be active in a patent [2] which appeared during the course of this work.

[1] Ainley, *J.*, 1953, 59.
[2] Curd and Young, Imperial Chemical Industries Limited, B.P. 696,692/1953.
[3] Berg, *J.*, 1961, 4041.
[4] Borsche, Diacont, and Hanau, *Ber.*, 1934, **67**, 676.
[5] Atkinson, Simpson, and Brown, *J.*, 1956, 1081.

large-scale preparations, but was better effected with 2,4-dibromo-5,5-dimethylhydantoin [6] in boiling chlorobenzene, and the product was converted directly into 1,2-dihydro-7-nitro-1-oxophthalazine (IV; R = R′ = H, X = O) by alkaline hydrolysis followed by treatment with hydrazine. The oxo-compound with phosphorus oxychloride–diethylaniline gave a better yield of the chloro-compound (V; R = Cl, R′ = H, R″ = $NO_2$) than was obtained by the method of Atkinson *et al.*[5] It was converted into the amine (V; R = $NH_2$, R′ = H, R″ = $NO_2$) by the published procedure.[5] In an alternative route, the phthalazone (IV; R = R′ = H, X = O) was treated with phosphorus pentasulphide in pyridine, affording the thiol (V; R = SH, R′ = H, R″ = $NO_2$), which with methyl sulphate in aqueous sodium hydroxide gave a mixture of *N*- and *S*-methyl derivatives. The *N*-methyl compound (IV; R = Me, R′ = H, X = S), which predominated, was separated by fractional crystallisation and was shown to be identical with an authentic specimen prepared from the phthalazone (IV; R = Me, R′ = H, X = O). When the methylation was effected with methyl iodide and sodium methoxide in anhydrous methanol, the *S*-methyl isomer (V; R = SMe, R′ = H, R″ = $NO_2$) predominated. Fusion of the S-methyl isomer with ammonium acetate gave the pure nitro-amine (V; R = $NH_2$, R′ = H, R″ = $NO_2$), but the crude mixture could also be used. This nitro-amine was also obtained by reaction of the thiol (V; R = SH, R′ = H, R″ = $NO_2$) with ammonium acetate and mercuric acetate. The nitro-amine was quaternised and the product was reduced to the methiodide (VI; R = Me, R′ = H, R″ = $NH_2$, X = I).




+ — denotes attachment to one of the ring-N.

Reaction of 1,2-dihydro-4-methyl-7-nitro-1-oxophthalazine [7] (IV; R = H, R′ = Me, X = O) with phosphorus oxychloride gave the chloro-compound (V; R = Cl, R′ = Me, R″ = $NO_2$), which was converted *via* the 4-phenoxy-derivative into 4-amino-1-methyl-6-nitrophthalazine (V; R = $NH_2$, R′ = Me, R″ = $NO_2$). The methyl methosulphate was prepared, and was treated with ammonia to give a base which on trituration with ethereal hydrogen chloride gave the methochloride (VI; R = R′ = Me, R″ = $NO_2$, X = Cl). The corresponding ethiodide (VI; R = Et, R′ = Me, R″ = $NO_2$, X = I), prepared directly with ethyl iodide, was reduced to the amine (VI; R = Et, R′ = Me, R″ = $NH_2$, X = I). The parent base, 4,6-diamino-1-methylphthalazine (V; R = R″ = $NH_2$, R′ = Me), was obtained by reduction of the nitro-compound (V; R = $NH_2$, R′ = Me, R″ = $NO_2$).

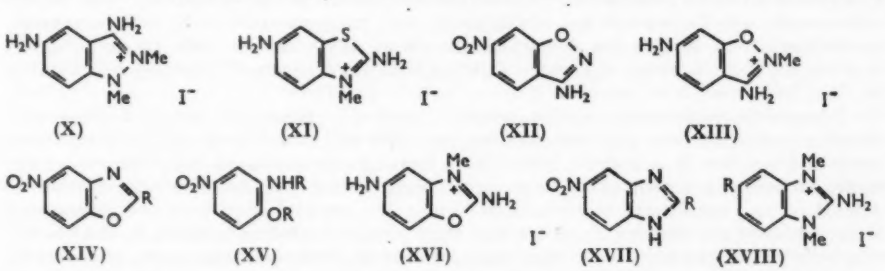
Attention was then turned from the phthalazines to the isomeric quinoxalines. Wolff *et al.*[8] condensed 4-nitro-1,2-phenylenediamine with butyl glyoxylate to give a mixture of isomeric quinoxalones. The corresponding chloro-compounds (VII; R = Cl, R′ = H, R″ = $NO_2$, or R = H, R′ = Cl, R″ = $NO_2$) were separated but structures were not assigned to the individual isomers. We find that partial reduction of 2,4-dinitrophenylglycine gives 1,2,3,4-tetrahydro-7-nitroquinoxal-2-one (VIII) which on conversion into the chloro-derivative with concomitant oxidation affords the compound (VII; R = Cl,

[6] Orazi and Meseri, *Anales Asoc. quim. argentina*, 1950, **38**, 307.
[7] Tirouflet, *Bull. Soc. Sci. Bretagne*, 1951, **26**, 7.
[8] Wolff, Pfister, Beutel, Wilson, Robinson, and Stevens, *J. Amer. Chem. Soc.*, 1949, **71**, 6.

R′ = H, R″ = $NO_2$). Since this work was completed, Cheeseman [9] has also prepared this chloro-compound by an unambiguous synthesis from 2-hydroxyquinazoline. The corresponding amine (VII; R = $NH_2$, R′ = H, R″ = $NO_2$) could not be quaternised or satisfactorily reduced. The known diamine [10] (VII; R = R″ = $NH_2$, R′ = H) was therefore converted into the diacetyl derivative and quaternised by fusion with methyl toluene-*p*-sulphonate. Hydrolysis of the corresponding iodide to the required diamine (IX) was accomplished only in very poor yield. The diamine (VII; R = R″ = $NH_2$, R′ = H) was therefore condensed with 2-amino-4-chloro-6-methylpyrimidine (III) but attempts to quaternise the resulting base failed.

Some compounds containing 5-membered heterocyclic rings were then synthesised. Reduction of 3-amino-1,2-dimethyl-5-nitroindazolium iodide [11] gave the corresponding diamine (X). The benzothiazole analogue (XI) and the corresponding ethiodide were obtained by quaternisation of 6-acetamido-2-aminobenzothiazole [12] followed by hydrolysis. 3-Amino-6-nitro-1,2-benzisoxazole (XII) was prepared by a modification of the method of Lindemann and Cissée [13] and was converted into the methiodide (through the methosulphate) and thence by reduction into 3,6-diamino-2-methyl-1,2-benzisoxazolium iodide (XIII).

2-Amino-5-nitrobenzoxazole (XIV; R = $NH_2$) was obtained by the reaction of 2-amino-4-nitrophenol with cyanogen bromide (cf. Pierron [14]). Fusion of 2-mercapto-5-nitrobenzoxazole (XIV; R = SH) with ammonium acetate and mercuric acetate gave a product whose analysis and chemical properties were consistent with its being the guanidine [XV; R = C(:NH)·$NH_2$], which on being heated lost ammonia to give compound (XIV;




R = $NH_2$). This aminobenzoxazole was soluble in dilute acid, but insoluble in 2N-aqueous sodium carbonate. Unexpectedly, it dissolved in 2N-aqueous sodium hydroxide, but was precipitated unchanged by acid. The possibility that this substance has the structure (XV; R = CN) was excluded by the absence of a band at 2200 $cm.^{-1}$ in the infrared spectrum (CN group), although it is possible that it passes into the phenol (XV; R = CN) in alkaline solution. Reduction of the methiodide of the nitrobenzoxazole (XIV; R = $NH_2$) afforded 2,5-diamino-3-methylbenzoxazolium iodide (XVI).

Kym and Ratner [15] have claimed the preparation of the amine (XVII; R = $NH_2$), m. p. 189—190°, by amination of the corresponding chloro-compound, which they obtained in poor yield from 5-nitrobenzimidazol-2-one. We were unable to repeat these preparations, but obtained the amine, m. p. 222—223° (decomp.), from 4-nitro-1,2-phenylenediamine and cyanogen bromide. On methylation it gave a mixture of two isomers; quaternisation of the mixture yielded 2-amino-1,3-dimethyl-5-nitrobenzimidazolium iodide (XVIII; R = $NO_2$) which was reduced to the diamine (XVIII; R = $NH_2$).

[9] Cheeseman, *J.*, 1961, 1246.
[10] Osdene and Timmis, *J.*, 1955, 2027.
[11] Parnell, *J.*, 1959, 2363.
[12] Kaufmann and Schultz, *Arch. Pharm.*, 1935, **273**, 31.
[13] Lindemann and Cissée, *Annalen*, 1929, **469**, 44.
[14] Pierron, *Ann. Chim. Phys.*, 1908, **15**, 191.
[15] Kym and Ratner, *Ber.*, 1912, **45**, 3258.

During this work an improved preparation of 2-amino-4-chloro-1-ethyl-6-methylpyrimidinium iodide [16] was developed.

## Experimental

*4,6-Diamino-2-methylquinazoline.*—4-Amino-2-methyl-6-nitroquinazoline (48 g.) was suspended in methanol (800 ml.) and hydrogenated over Adams catalyst (4 g.) (uptake 16·15 l. in 2 hr.; 87·5%). After the catalyst had been filtered off, the green solution was evaporated *in vacuo*. A solution of the residue in 2N-acetic acid (350 ml.) was filtered through charcoal and basified (phenolphthalein) at 10—20° with 2N-sodium hydroxide. The yellow, crystalline *diamine* (36 g., 88%) was filtered off; a sample (1 g.), m. p. 240—245°, crystallised from water (25 ml.) as pale brown needles (0·7 g.), m. p. 244—246° (Found: C, 51·1; H, 6·8; N, 26·9; $H_2O$, 17·4. $C_9H_{10}N_4,2H_2O$ requires C, 51·45; H, 6·7; N, 26·65; $H_2O$, 17·1%).

*2-Amino-4-(4-amino-2-methylquinazol-6-ylamino)-6-methylpyrimidine.*—4,6-Diamino-2-methylquinazoline (21 g.), 2-amino-4-chloro-6-methylpyrimidine (18 g.), water (250 ml.), and concentrated hydrochloric acid (7·5 ml.) were refluxed together for 1 hr. The solution was diluted with water (400 ml.), cooled in ice, and basified at 10—15° with 2N-sodium hydroxide. The precipitate was filtered off and crystallised as yellow needles (29 g., 80·5%), m. p. 343—344°, from aqueous methanol (Found: C, 59·4; H, 5·3; N, 34·75. $C_{14}H_{15}N_7$ requires C, 59·8; H, 5·35; N, 34·8%).

This base (5 g.) and methyl toluene-*p*-sulphonate (8·5 g.) were melted together and kept at 150° for 0·5 hr. After being cooled, the hygroscopic solid was powdered under acetone, and the solid was quickly filtered off and dried over silica gel. The product from eight similar fusions was dissolved in hot water (2 l.), and sodium chloride (600 g.) was added. The resulting yellow solid was filtered off and crystallised from 2N-acetic acid (1 l.) and concentrated hydrochloric acid, to give the *dimethochloride* (29 g., 46%), m. p. >360° (Found: C, 46·1; H, 5·85; Cl, 17·1; N, 23·75; $H_2O$, 8·9. $C_{16}H_{21}Cl_2N_7O_2,2H_2O$ requires C, 45·9; H, 6·0; Cl, 16·95; N, 23·4; $H_2O$, 8·6%).

*3-Bromo-6-nitrophthalide.*—6-Nitrophthalide (25·5 g.) (Borsche *et al.*[4]), 2,4-dibromo-5,5-dimethylhydantoin (21·2 g.), and chlorobenzene (210 ml.) were illuminated with a tungsten lamp and refluxed in a bath at 160—170°. Heating was continued until the evolution of hydrogen bromide ceased (6—8 hr.). After being cooled, the 5,5-dimethylhydantoin was filtered off and the filtrate evaporated *in vacuo*. The residual gums from four preparations were combined and distilled at *ca.* 0·3 mm. from a retort heated in an air-bath at 185—190°. The pale yellow distillate, containing some crystals of 5,5-dimethylhydantoin, was dissolved in dry benzene (450 ml.). Next day the solution was filtered, and evaporation *in vacuo* gave the product (100—112 g., 71—78·5%) which did not solidify. Borsche *et al.*[4] described it as a yellow glass, m. p. *ca.* 90°.

*1,2-Dihydro-7-nitro-1-oxophthalazine.*—3-Bromo-6-nitrophthalide (105·5 g.) in water (1055 ml.) was refluxed for 45 min. and sodium hydroxide (49 g.) in water (440 ml.) was added to the nearly clear solution, cooled to 60—70°. The red solution was filtered and mixed with hydrazine sulphate (54·5 g.) in water (3040 ml.) at 50—60°. The solution was treated with 2N-sodium hydroxide until just alkaline to litmus and then immediately adjusted to pH *ca.* 4 by addition of acetic acid. After being stirred at 60° for 15 min. the granular, yellow solid (41—53 g., 50—65%), m. p. 224—227°, was filtered off. Crystallisation from water or anisole gave the product as pale yellow needles, m. p. 237—239° (Atkinson *et al.*[5] give m. p. 232—233°) (Found: C, 50·55; H, 2·65; N, 22·2. Calc. for $C_8H_5N_3O_3$: C, 50·25; H, 2·6; N, 22·0%).

*1-Mercapto-7-nitrophthalazine.*—To a stirred suspension of 1,2-dihydro-7-nitro-1-oxophthalazine (20 g.) in anhydrous pyridine (100 ml.) was added phosphorus pentasulphide (24 g.). The mixture was stirred and heated at 100° for 1·5 hr. and the solution was then poured into water (1 l.). The sticky solid, which soon hardened, was filtered off, dissolved in 0·1N-sodium hydroxide (2 l.), and filtered through charcoal from sulphur. The filtrate was acidified with acetic acid, and the *product* (13·5—15·2 g., 62·5—70%), m. p. 222—225°, collected (Found: C, 46·95; H, 2·7; N, 19·95; S, 15·2. $C_8H_5N_3O_2S$ requires C, 46·4; H, 2·4; N, 20·3; S, 15·5%).

*Methylation of 1-Mercapto-7-nitrophthalazine.*—(*a*) A solution of N-sodium ethoxide (245 ml.) was added to a fine suspension of 1-mercapto-7-nitrophthalazine in dry ethanol (~ 1·1 l.), followed by methyl iodide (14·5 ml.), and the mixture was refluxed for 1 hr. The clear solution

was evaporated *in vacuo*, and the residue treated with water, filtered off, and washed with 0·1N-sodium hydroxide and finally water. This product (48 g., 82·5%), m. p. 142—146°, was a mixture of *S*- and *N*-methylated products which were not easily separated. However, in one experiment the S-*methyl isomer* predominated and was purified by crystallisation from benzene–light petroleum (b. p. 60—80°) and then from ethanol as felted yellow needles, m. p. 180—181° (Found: C, 48·25; H, 3·65; N, 19·3; S, 15·5. $C_9H_7N_3O_2S$ requires C, 48·9; H, 3·2; N, 19·0; S, 14·5%).

(*b*) 1-Mercapto-7-nitrophthalazine (1 g.) in water (20 ml.) containing sodium hydroxide (0·425 g.) was stirred with methyl sulphate (0·53 ml.) for 1 hr., and the yellow precipitate was filtered off, washed with 0·1N-sodium hydroxide and water, and dried. Crystallisation from benzene–light petroleum (b. p. 60—80°) gave the crude *product* (0·7 g.), m. p. 135—150° (decomp.). Several recrystallisations from benzene–light petroleum (b. p. 60—80°) gave the pure *N*-methyl isomer as orange prisms, m. p. 161—162° (decomp.), not depressed by authentic 1,2-dihydro-2-methyl-7-nitro-4-thiophthalazine. This product depressed the m. p. of the higher-melting isomer obtained in method (*a*).

1,2-*Dihydro*-2-*methyl*-7-*nitro*-1-*thiophthalazine*.—1,2-Dihydro-2-methyl-7-nitro-1-oxophthalazine (1·25 g.) (Atkinson *et al.*[5]), phosphorus pentasulphide (1·5 g.), and anhydrous pyridine (6·25 ml.) were stirred on the steam bath for 1·5 hr. The suspension was added to ice-water (100 ml.), and the yellow, granular solid was filtered off, washed with water, and dried. The crude product (2·3 g.) was extracted with benzene (50 ml.), and the extract concentrated to about 15 ml. After being cooled, unchanged material (0·9 g.), m. p. 177—179°, was filtered off, and evaporation of the filtrate gave the orange *thione* (0·3 g.), which crystallised from light petroleum as yellow prisms (0·2 g.), m. p. 160—162° (decomp.) (Found: C, 49·2; H, 3·45; S, 14·35. $C_9H_7N_3O_2S$ requires C, 48·9; H, 3·2; S, 14·5%).

1-*Chloro*-7-*nitrophthalazine*.—1,2-Dihydro-7-nitro-1-oxophthalazine (5 g.), diethylaniline (4·45 ml.), and redistilled phosphorus oxychloride (25 ml.) were heated on the steam bath for 20 min., a yellow-brown solution being formed. This was refluxed until a deep red colour started to appear (*ca.* 5 min.); the solution was then rapidly cooled and poured on ice (*ca.* 500 g.). The mixture was stirred with charcoal, then filtered and basified at $<10°$ with 50% w/w aqueous sodium hydroxide. The precipitate was collected and resuspended in iced water to remove phosphate. After being dried the product was triturated with light petroleum (b. p. 40—60°) and was obtained as a buff solid (2·9 g., 53%), m. p. 156—159° (decomp.) (Atkinson *et al.*[5] give m. p. 155—157°). Attempts to crystallise the product caused decomposition.

1-*Amino*-7-*nitrophthalazine*.—(*a*) Ammonium acetate (80 g.) and the mixture of methylation products of 1-mercapto-7-nitrophthalazine [8 g. prepared by method (*a*)] were melted at *ca.* 160° (internal temperature 130—135°) for 0·75 hr. The melt was cooled and poured into water (800 c.c.), and the suspension basified (phenolphthalein) with 50% w/w aqueous sodium hydroxide. The solid was filtered off and dissolved at 60° in 2N-acetic acid (200 ml.); this solution was filtered and basified with 50% w/w aqueous sodium hydroxide; the orange precipitate formed yellow crystals (1·7 g.), m. p. 306—308° (decomp.), from dimethylformamide. Crystallisation from ethanol gave felted orange needles, m. p. 309—310° (decomp.) (Found: C, 50·2; H, 2·9; N, 29·8. Calc. for $C_9H_6N_4O_2$: C, 50·5; H, 3·15; N, 29·5%). [Atkinson *et al.*[5] give m. p. 303—304° (decomp.).]

(*b*) 1-Mercapto-7-nitrophthalazine (1 g.), mercuric acetate (1·6 g.), and ammonium acetate (10 g.) were melted and kept at 140° (internal temperature) for 0·5 hr. The melt was heated with 2N-acetic acid (20 ml.) at *ca.* 90° for 5 min., filtered from mercuric sulphide, and basified with concentrated aqueous ammonia. The precipitate crystallised from aqueous dimethylformamide as orange needles (0·35 g., 38%), m. p. 313—315° (decomp.), identical with an authentic specimen of the nitro-amine.

1-*Methylamino*-7-*nitrophthalazine*.—1-Mercapto-7-nitrophthalazine (1 g.), mercuric chloride (2·7 g.), and methylamine (10 ml.) were mixed and kept in a sealed tube at 25—30° for 24 hr. The excess of methylamine was then evaporated, the residue ground with water (100 ml.), and the suspension saturated with hydrogen sulphide. The black mixture was heated to 80°, then filtered and basified at 10—20° with concentrated aqueous ammonia. The yellow precipitate was filtered off, washed with water, and dissolved in hot 2N-hydrochloric acid (15 ml.). The hydrochloride which crystallised was filtered off, washed with acetone, and dissolved in warm water (15 ml.). The solution was treated with charcoal, then filtered and basified while

hot with concentrated aqueous ammonia, to give the *methylamino-compound* (0·4 g., 40%) that crystallised from aqueous dimethylformamide as pale yellow needles, m. p. 220—223° (decomp.) (Found: C, 52·7; H, 4·1; N, 27·1. $C_9H_8N_4O_2$ requires C, 52·95; H, 3·9; N, 27·45%).

1-*Amino*-7-*nitrophthalazine Methiodide*.—A suspension of 1-amino-7-nitrophthalazine (12·4 g.) in dry nitrobenzene (248 ml.) was heated with methyl sulphate (6·5 ml.) on the steam-bath for 3 hr. The mixture was cooled in ice and filtered, and the residue washed with ether. Crystallisation from methanol gave yellow needles (12·3 g.), m. p. 255—257° (decomp.), which were dissolved in boiling water (350 ml.); potassium iodide (150 g.) was added. The iodide separated as red needles (11·2 g., 52%), m. p. 268—270° (decomp.), identical with the product prepared by the method of Atkinson *et al.*[5]

1,7-*Diaminophthalazine Methiodide*.—1-Amino-7-nitrophthalazine methiodide (11·2 g.) was shaken in methanol (336 ml.) with Adams catalyst (1·12 g.) and hydrogen at atmospheric pressure with intermittent warming to *ca.* 40°. The reduction required *ca.* 7 hr. The solution was then boiled, filtered, and evaporated *in vacuo*. Crystallisation of the residue from aqueous potassium iodide gave the *methiodide* (7·8 g., 77%) as pale brown plates, m. p. 297—299° (decomp.) (Found: I, 39·9; N, 17·4; $H_2O$, 5·9. $C_9H_{11}IN_4,H_2O$ requires I, 39·6; N, 17·5; $H_2O$, 5·6%).

4-*Chloro*-1-*methyl*-6-*nitrophthalazine*.—1,2-Dihydro-4-methyl-7-nitro-1-oxophthalazine (10 g.) and redistilled phosphorus oxychloride (50 ml.) were refluxed for 0·25 hr., cooled in ice, and added to ice-water (750 ml.). The suspension was filtered (charcoal) and the filtrate basified to pH 10·0 with 50% w/w aqueous sodium hydroxide at 5—20°. The pink solid (8 g., 73·5%) which separated decomposed at 160—161°, after shrinking at 140°. Attempts to crystallise the product caused decomposition.

4-*Amino*-1-*methyl*-6-*nitrophthalazine*.—4-Chloro-1-methyl-6-nitrophthalazine (15 g.), ammonium carbonate (60 g.), and phenol (120 g.) were heated on the steam-bath for 0·75 hr. The solution so obtained was cooled in ice, mixed with ice-water (600 ml.), and basified (phenolphthalein) with 50% w/w aqueous sodium hydroxide at 0—10°. The brown precipitate was filtered off and washed with 2N-sodium hydroxide and water. The solid (19·5 g.), m. p. 215—220° (decomp.), was mainly 1-methyl-6-nitro-4-phenoxyphthalazine. It was added to ammonium acetate (90 g.) preheated to 180—185°. A clear red solution was obtained after 0·25 hr.; this was cooled in ice and treated with ice-water (600 ml.). The gummy mixture was basified (phenolphthalein) with 50% w/w aqueous sodium hydroxide at 0—10°, and the yellow solid was filtered off and washed with water. The damp cake was dissolved in 2N-acetic acid (450 ml.), and the filtrate was basified (phenolphthalein) with 50% w/w aqueous sodium hydroxide at 0—10°. The yellow *amine* (10·5 g., 73·5%), m. p. 274—275° (decomp.), was used without further purification. A sample crystallised from ethanol as yellow needles, m. p. 282° (decomp.) (Found: C, 52·7; H, 4·5; N, 27·0. $C_9H_8N_4O_2$ requires C, 52·95; H, 3·9; N, 27·45%).

The amine (1 g.) with methyl sulphate (0·62 g., 0·47 ml.) in nitrobenzene (10 ml.), gave the *methosulphate*, isolated as the *methochloride* (0·8 g., 64%) which crystallised from methanol–acetone as pink needles, m. p. 310—312° (decomp.) (Found: Cl, 14·2; N, 21·7. $C_{10}H_{11}ClN_4O_2$ requires Cl, 13·95; N, 22·0%).

The amine (15 g.), ethyl iodide (30 ml.), and 2-ethoxyethanol (150 ml.) were heated on the steam-bath for 5 hr., to give the *ethiodide* (11·2 g., 42%), orange needles, m. p. 283—285° (decomp.) (from water) (Found: I, 35·1; N, 15·6. $C_{11}H_{13}IN_4O_2$ requires I, 35·3; N, 15·5%).

4,6-*Diamino*-1-*methyl phthalazine*.—4-Amino-1-methyl-6-nitrophthalazine (10 g.) in 3N-acetic acid (200 ml.) was hydrogenated at atmospheric pressure (Adams catalyst, 1 g.: uptake 89% in 4·5 hr.). The suspension was filtered and the filtrate basified (phenolphthalein) at 0—10° with 50% w/w aqueous sodium hydroxide. The *p roduct* (9 g.) crystallised from water (100 ml.) as brown needles (7 g., 82%), m. p. 274—275° (d ecomp.) (Found: C, 62·0; H, 5·9; N, 31·8. $C_9H_{10}N_4$ requires C, 62·05; H, 5·75; N, 32·2%).

4,6-*Diamino*-1-*methylphthalazine Ethiodide*.—4-Am ino-1-methyl-6-nitrophthalazine ethiodide (8 g.), suspended in ethanol (100 ml.), was similarly reduced (catalyst 0·8 g.; uptake 100% in 1 hr.). The suspension was warmed to effect solution and the catalyst was filtered off. When the filtrate was cooled in ice, the *ethiodide* (6 g., 82%) separated as brown prisms, m. p. 293—295° (decomp.) (Found: I, 38·2; N, 17·0. $C_{11}H_{15}IN_4$ requires I, 38·5; N, 17·0%).

2-*Amino*-4-(4-*amino*-1-*methylphthalazin*-6-*ylamino*)-6-*methylpyrimidine*.—4,6-Diami no-1-methylphthalazine (8 g.), 2-amino-4-chloro-6-methylpyrimidine (7 g.), and water (100 ml.)

containing concentrated hydrochloric acid (3 ml.) were refluxed for 1 hr. The hot solution was diluted with water (200 ml.), cooled to 5—10°, and basified (phenolphthalein) with 50% w/w aqueous sodium hydroxide. The pink solid which crystallised was filtered off and recrystallised from aqueous pyridine (500 ml. containing 100 ml. of pyridine). The *product* (11·3 g., 91%) separated as grey needles, m. p. 315—316° (decomp.) (softens at 181—184°) (Found: C, 55·85; H, 5·8; N, 32·6. $C_{14}H_{15}N_7,H_2O$ requires C, 56·1; H, 5·7; N, 32·75%).

This base (9 g.) was heated in nitrobenzene (150 ml.) with methyl sulphate (5·7 ml.) on the steam bath for 3 hr. After being cooled to 20°, the crude bismethosulphate was filtered off, washed with acetone, dissolved in water (300 ml.), treated with charcoal, and filtered. The filtrate was neutralised (litmus) with sodium hydrogen carbonate. Addition of sodium chloride caused the dimethochloride to crystallise. After being cooled in ice, the white solid was filtered off, washed with brine, and dissolved in warm 2N-acetic acid (300 ml.). Concentrated hydrochloric acid (30 ml.) was added to the filtered solution; the *dimethochloride* (8·5 g., 60·5%) separated as white needles, m. p. 322—324° (decomp.) (Found: Cl, 17·0; N, 24·25; $H_2O$, 6·3. $C_{16}H_{21}Cl_2N_7,1{\cdot}5H_2O$ requires Cl, 17·3; N, 23·95; $H_2O$, 6·6%).

*2-Amino-4-chloro-6-methylpyrimidine Ethiodide.*—2-Amino-4-chloro-6-methylpyrimidine (100 g.), ethyl sulphate (130 ml.), and dry nitrobenzene (200 ml.) were heated on the steam-bath for 16 hr. The cooled dark solution was mixed with ether (300 ml.) and extracted with water (3 × 100 ml.). After being washed with ether, the aqueous extract was neutralised with solid sodium hydrogen carbonate, a solid separating; this was starting material (30 g.). The filtrate was heated to *ca.* 60°, and sodium iodide (360 g.) added; cooling in ice caused the quaternary salt to separate as orange prisms (59 g.) containing some sodium iodide. This crystallised from 90% aqueous ethanol to give the product (25 g., 23·8% based on unrecovered starting material), m. p. 234—235° (decomp.) (Found: I, 42·3; N, 14·0; total halogen, 126·5 as AgX. Calc. for $C_7H_{11}ClIN$: I, 42·1; N, 13·7; total halogen as AgX, 125·0%). This product did not depress the m. p. of an authentic sample prepared by Stacey's method.[16]

*3,5-Diamino-1,2-dimethylindazolium Iodide.*—3-Amino-1,2-dimethyl-5-nitroindazolium iodide [11] (9·3 g.) was suspended in methanol (186 ml.) with Adams catalyst (0·93 g.) and hydrogenated at room temperature and pressure. Absorption of the theoretical quantity of hydrogen was complete in 0·3 hr. during which time the starting material dissolved and the product separated. The product was redissolved by warming the mixture to *ca.* 30° and the catalyst was filtered off. Treatment of the filtrate with ether (*ca.* 750 ml.) gave the *diamine* as buff crystals (7·3 g., 83%), m. p. 246—248° (decomp.) (from methanol) (Found: I, 41·2; N, 18·2. $C_9H_{13}IN_4$ requires I, 41·8; N, 18·4%).

*6-Acetamido-2-amino-3-methylbenzothiazolium Iodide.*—6-Acetamido-2-aminobenzothiazole [12] (30 g.) in boiling methanol (450 ml.) was refluxed overnight with methyl iodide (30 ml.). A solid which separated was filtered off [22·3 g., 44·5%; m. p. 310—314° (decomp.)]. Treatment of the mother liquor with an equal volume of ether gave a further crop (6·7 g., 12·5%), m. p. 303—307° (decomp.). The quaternary salt crystallised from water as buff blades, m. p. 311—313° (decomp.) (Found: I, 36·1; N, 12·3; S, 9·3. $C_{10}H_{12}IN_3OS$ requires I, 36·4; N, 12·1; S, 9·2%). The *ethiodide* was prepared similarly as white needles (from ethanol–ether), m. p. 230—234° (decomp.) (Found: I, 35·8; N, 11·6. $C_{11}H_{14}IN_3OS$ requires I, 35·0; N, 11·6%).

*2,6-Diamino-3-methylbenzothiazolium Iodide.*—The foregoing acetyl compound (29 g.) in N-hydrochloric acid (290 ml.) was refluxed for 1 hr. The cooled solution was neutralised with solid sodium hydrogen carbonate, then warmed to 90°, and sodium iodide (58 g.) was added. After being cooled, the *product* (23 g., 90%) was filtered off; it crystallised from water as pale yellow needles, m. p. 271—273° (decomp.) (Found: I, 41·6; N, 13·9; S, 10·7. $C_8H_{10}IN_3S$ requires I, 41·3; N, 13·7; S, 10·4%). The *ethiodide* was similarly prepared as white prisms (from ethanol–ether), m. p. 235—236° (decomp.) (Found: I, 39·4; N, 13·8. $C_9H_{12}IN_3S$ requires I, 39·6; N, 13·1%).

*6-Nitro-1,2-benzisoxazole-3-carboxhydrazide.*—3-Methoxycarbonyl-6-nitrobenzisoxazole (48 g.) was heated in hot ethanol (1160 ml.) with hydrazine hydrate (13·4 ml.) for 0·5 hr., then cooled in ice, and the product (36 g., 75%) which separated was filtered off; it had m. p. 174—177° (Lindemann and Cissée [13] give m. p. 170°).

The hydrazide (25 g.) was ground in a mortar with concentrated hydrochloric acid (75 ml.) and washed with water (75 ml.) on to ice (75 g.). Sodium nitrite (12·5 g.) in water (63·5 ml.)

[16] Stacey, Imperial Chemical Industries Limited, B.P. 674,259/1952.

was added all at once, and the whole was shaken for 5—10 min. The hydrazide was converted into a bulky solid which was filtered off, washed with water, and dried *in vacuo* to give the azide (24·5 g., 94%), decomp. *ca.* 90°.

3-*Benzyloxycarbonylamino*-6-*nitro*-1,2-*benzisoxazole*.—The azide (15 g.), anhydrous toluene (150 ml.), and benzyl alcohol (7·5 ml.) were mixed together and heated carefully. An exothermic reaction occurred with evolution of nitrogen, and after the reaction had subsided the solution was refluxed for a further 0·3 hr. After being cooled, the *product* (15 g., 74·5%), m. p. 189—191° (sinters at 175°), was filtered off; it crystallised from ethanol as plates, m. p. 191—192·5° (Found: C, 57·3; H, 3·9; N, 13·3. $C_{15}H_{11}N_3O_5$ requires C, 57·5; H, 3·5; N, 13·4%).

3-*Amino*-6-*nitro*-1,2-*benzisoxazole*.—The above urethane (20 g.), suspended in acetic acid (60 ml.), was heated on the steam-bath whilst hydrogen bromide was passed in for 3 hr. The dark solution was poured into water (1 l.); the yellow precipitate of amine (10 g., 87%) melted at 220—224° (Lindemann and Cissée [18] give m. p. 234°). Crystallisation from methanol raised the m. p. to 234°.

The amine (17 g.) in dry nitrobenzene (170 ml.) was heated with methyl sulphate (9·9 ml.) on the steam-bath for 1·5 hr., cooled, and poured into ether (800 ml.). The solid was collected and dissolved in warm water (170 ml.); the solution was clarified with charcoal, and sodium iodide (65 g.) was added to the filtrate; the 3-*amino*-2-*methyl*-6-*nitro*-1,2-*benzisoxazolium iodide* (9·0 g., 50%) which separated crystallised from ethanol as pale yellow needles, m. p. 211—212° (decomp.) (Found: I, 39·8; N, 12·7. $C_9H_8IN_3O_3$ requires I, 39·6; N, 13·0%).

3,6-*Diamino*-2-*methyl*-1,2-*benzisoxazolium Iodide*.—3-Amino-2-methyl-6-nitro-1,2-benzisoxazolium iodide (16·4 g.) was hydrogenated in methanol (328 ml.) with Adams catalyst (1·64 g.) at room temperature and pressure. After removal of the catalyst the solution was poured into ether (1·3 l.). The *product* was precipitated as a cream solid (11·6 g., 78%), m. p. 239—241° (decomp.), which crystallised from aqueous sodium iodide as cream needles, m. p. 244° (decomp.) (Found: I, 42·4; N, 13·9. $C_9H_{10}IN_3O,0{\cdot}5H_2O$ requires I, 42·2; N, 13·95%).

2-*Amino*-5-*nitrobenzoxazole*.—2-Amino-4-nitrophenol (76·5 g.) was dissolved in ethanol (190 ml.) and diluted with water (190 ml.). To this supersaturated solution was added cyanogen bromide (54·5 g.), and the mixture was mechanically shaken overnight. The fine yellow solid was filtered off and stirred with hot water; the mixture was filtered and the solid (66·5 g.) had m. p. 290—295° (decomp.). Crystallisation from dimethylformamide (270 ml.) gave the *product* as minute yellow needles (51·5 g., 64%), m. p. 304° (decomp.) (Found: C, 47·3; H, 3·2; N, 23·0. $C_7H_5N_3O_3$ requires C, 47·0; H, 2·8; N, 23·4%). It was soluble in 2N-hydrochloric acid and 2N-sodium hydroxide, insoluble in 2N-acetic acid and 2N-sodium carbonate.

2-*Guanidino*-4-*nitrophenol*.—2-Mercapto-5-nitrobenzoxazole [17] (2 g.), mercuric acetate (3·3 g.), and ammonium acetate (10 g.) were melted at 160° (internal temperature 150°) for 0·5 hr. The cooled melt was mixed with 2N-acetic acid (20 ml.), warmed to 60°, and then filtered. Basification with concentrated aqueous ammonia gave the *product* as yellow needles (0·9 g.), m. p. 300° (decomp.) (changes form at 270°). After being purified by precipitation from acetic acid the compound had m. p. 303—304° (decomp.) (Found: C, 43·1; H, 4·3; N, 28·0. $C_7H_6N_4O_3$ requires C, 43·8; H, 4·1; N, 28·5%).

2-*Amino*-5-*nitrobenzoxazole from* 2-*Guanidino*-4-*nitrophenol*.—2-Guanidino-4-nitrophenol (1 g.) was heated at 280° for 0·5 hr., ammonia being evolved. The cooled solid was triturated with 2N-acetic acid and filtered off. After precipitation from 2N-hydrochloric acid with sodium hydrogen carbonate, the product (0·4 g.) had m. p. 304° (decomp.) undepressed on admixture with the material described above.

2-*Amino*-3-*methyl*-5-*nitrobenzoxazolium Iodide*.—To 2-amino-5-nitrobenzoxazole (18 g.) with methyl sulphate (10·4 ml.) in dry nitrobenzene (180 ml.) at 150° (0·5 hr.) gave, after normal treatment an *iodide* (15·3 g., 47%), yellow prisms, decomp. 205—210° (Found: I, 39·85; N, 13·1. $C_9H_8IN_3O_3$ requires I, 39·6; N, 12·8%).

2,5-*Diamino*-3-*methylbenzoxazolium Iodide*.—The foregoing salt (5 g.) was hydrogenated in methanol (150 ml.) as above. The gummy product was dissolved in water for further use.

2-*Amino*-5-*nitrobenzimidazole*.—To 4-nitro-1,2-phenylenediamine (40·5 g.) in dioxan (648 ml.) and water (162 ml.) was added cyanogen bromide (28·4 g.), and the mixture was shaken overnight and then evaporated *in vacuo*. The residual solid was treated with 1·2N-sodium hydroxide

[17] Deck and Dains, *J. Amer. Chem. Soc.*, 1933, **55**, 4986.

(500 ml.) at 60°. The mixture was filtered (charcoal) and kept at 60° whilst ammonium chloride (17 g.) in water (100 ml.) was added. After being cooled, the *product* (34 g., 72%), m. p. 220—223° (decomp.), crystallised as yellow needles. It recrystallised from water as a hemihydrate, m. p. 222—223° (decomp.) (Found: C, 45·0; H, 3·85; N, 30·0; $H_2O$, 5·0. Calc. for $C_7H_6N_4O_2,0{\cdot}5H_2O$: C, 44·9; H, 3·7; N, 30·0; $H_2O$, 4·8%) [Kym and Ratner [15] give m. p. 189—190°].

*Methylation of 2-Amino-5-nitrobenzimidazole.*—The base (27 g.) with methyl sulphate (21·6 ml.) in 2N-sodium hydroxide (227 ml.) gave a mixture (22·3 g., 76·5%), m. p. 257—307° (decomp.), of two *N*-methylbenzimidazoles that was used without separation to give a single quaternary salt (see below).

*2-Amino-1,3-dimethyl-5-nitrobenzimidazolium Iodide.*—To the foregoing mixture (22·3 g.) in anhydrous nitrobenzene (223 ml.) at 150° was added methyl sulphate (12·3 ml.). After 0·25 hr. the mixture was cooled, and acetone (670 ml.) was added. The resultant crystals were filtered off, washed with acetone, and dissolved in warm water (117 ml.). Sodium iodide (30 g.) was added. The *di-iodide* (26·0 g., 67%) which separated was filtered off; it crystallised from water as yellow prisms, m. p. 304—305° (decomp.) (Found: I, 38·1; N, 16·6. $C_9H_{11}I_2N_4O_2$ requires I, 38·0; N, 16·8%).

*2,5-Diamino-1,3-dimethylbenzimidazolium Iodide.*—2-Amino-1,3-dimethyl-5-nitrobenzimidazolium iodide (28·4 g.) was hydrogenated in methanol (568 ml.) as usual, to give a *diamine iodide* (87%) as colourless needles, m. p. 274—275° (decomp.) (from ethanol) (Found: I, 41·8; N, 18·3. $C_9H_{13}IN_4$ requires I, 41·8; N, 18·4%).

*1,2,3,4-Tetrahydro-7-nitro-2-oxoquinoxaline.*—To *N*-(2,4-dinitrophenyl)glycine [18] (10 g.) in methanol (200 ml.) was added sodium hydrogen carbonate (8·4 g.) dissolved in the minimum amount of water, and to the stirred suspension were added during 30 min. sodium sulphide nonahydrate (26 g.) and sodium hydrogen carbonate (8·4 g.) in water (60 ml.). An exothermic reaction occurred and the temperature rose to *ca.* 45°. After being stirred at room temperature for 4 hr. the mixture was cooled in ice and the precipitated sodium salts were filtered off and dissolved in warm water (700 ml.). After being filtered, the solution was acidified with acetic acid. The *product* (4·4 g., 55%) crystallised. It recrystallised from nitrobenzene as red plates with a bluish reflex, m. p. 262—264° (decomp.) (Found: C, 50·3; H, 3·75; N, 21·3. $C_8H_7N_3O_3$ requires C, 49·8; H, 3·6; N, 21·7%).

*2-Chloro-7-nitroquinoxaline.*—1,2,3,4-Tetrahydro-7-nitro-2-oxoquinoxaline (1·0 g.), phosphorus pentachloride (0·85 g.) and phosphorus oxychloride (6·5 ml.) were heated on the steam-bath for 1 hr. The cooled mixture was poured on ice; the dark brown solid which separated was filtered off and extracted with light petroleum (b. p. 60—80°) to give the product (0·2 g.), m. p. 190—193°, which crystallised from ethanol as slender cream needles, m. p. 193—194° identical with the compound, m. p. 191—193°, prepared by the method of Wolff *et al.*[8] (Found: C, 45·6; H, 2·2; Cl, 17·3. Calc. for $C_8H_4Cl_2N_3O_2$: C, 45·8; H, 1·9; Cl, 17·0%) (Cheeseman [9] gives m. p. 188—190°).

*3,6-Diacetamidoquinoxaline Methiodide.*—3,6-Diacetamidoquinoxaline [10] (6·0 g.) and methyl toluene-*p*-sulphonate (5·0 g.) were fused at 160° for 0·5 hr. Treating a solution of the product in hot water (180 ml.) with sodium iodide (40 g.) and crystallising the precipitate (6·6 g.) from aqueous sodium iodide or methanol gave the pure *methiodide*, m. p. 233—236° (decomp.) raised to 301—303° (decomp.) after drying at 100°/15 mm. (Found: I, 30·7; N, 13·5. $C_{13}H_{15}IN_4O_2,2H_2O$ requires I, 30·2; N, 13·25%).

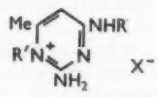
*3,6-Diaminoquinoxaline Methiodide.*—3,6-Diacetamidoquinoxaline methiodide (0·5 g.) and N-hydrochloric acid (5 ml.) were refluxed for 1 hr. The solution was filtered and neutralized with solid sodium hydrogen carbonate, and potassium iodide was added. The resultant brown solid (0·15 g.) was filtered off and washed with acetone. Crystallisation from aqueous sodium iodide gave the *diamine methiodide* as bronze plates, m. p. 233—235° (decomp.) (Found: C, 34·0; H, 3·9; I, 39·9. $C_9H_{11}IN_4,H_2O$ requires C, 33·8; H, 3·75; I, 39·7%).

*2-Amino-4-(3-aminoquinoxalin-6-ylamino)-6-methylpyrimidine.*—3,6-Diaminoquinoxaline [10] (3·4 g.) and 2-amino-4-chloro-6-methylpyrimidine (3·4 g.) in 2N-hydrochloric acid (102 ml.) were refluxed for 1 hr. After addition of water, the solution was basified with 50% w/w aqueous sodium hydroxide, to give the *product* (5·0 g., 90%), which crystallised from aqueous ethanol as buff needles, m. p. 288—290° (decomp.) (Found: C, 51·1; H, 5·5; N, 33·3; $H_2O$, 11·9. $C_{13}H_{13}N_7,2H_2O$ requires C, 51·5; H, 6·3; N, 32·3; $H_2O$, 11·9%).

[18] Abderhalden and Blumberg, *Z. physiol. Chem.*, 1910, **65**, 319.

XUM

*Condensation of the Chloropyrimidine Quaternary Salt with the Heterocyclic Diamine Quaternary Salts. General Method.*—The chloropyrimidine quaternary iodide (0·1 mol.), and the diamine quaternary salt (0·1 mol.) in 2N-hydrochloric acid (50 ml.) and water (350 ml.) were refluxed

Bisquaternary salts. 

| No. | R and salt * | R′ | X | Yield (%) | Cryst. from | M. p. (decomp.) |
|---|---|---|---|---|---|---|
| 1 | 4-Amino-2-methylquinazol-6-yl, A † ... | Me | Cl | 70 | 2N-AcOH–HCl | ≮360° |
| 2 | 4-Aminophthalazin-6-yl, B ..... | Me | I | 100 | | 281—283 |
| 3 | ,, ,, A ..... | ,, | Cl | 87 | 2N-AcOH–HCl | 327 |
| 4 | 4-Amino-1-methylphthalazin-6-yl, D ... | Et | I | 47·5 | EtOH–$Et_2O$ | 305 |
| 5 | 3-Amino-1-methylindazol-6-yl, B ..... | Me | I | 91 | $H_2O$ | 261—263 |
| 6 | ,, ,, ,, A ..... | ,, | Cl | 73 | $H_2O$ | 271—272 |
| 7 | 2-Aminobenzothiazol-6-yl, A ..... | Me | Cl | 79 | $H_2O$ | 295—298 |
| 8 | ,, ,, D ..... | Et | I | 76·5 | $H_2O$ | 308—309 |
| 9 | ,, ,, C ..... | ,, | Cl | 64 | EtOH–$Et_2O$ | 273—275 |
| 10 | 3-Amino-1,2-benzisoxazol-6-yl, B ..... | Me | I | 56 | $H_2O$ | 235—245 |
| 11 | ,, ,, ,, A ..... | ,, | Cl | 47 | MeOH–$COMe_2$ | 260 |
| 12 | 2-Aminobenzoxazol-6-yl, B ..... | Me | I | 60 | Aq. NaI | 309—310 |
| 13 | 2-Amino-1-methylbenzimidazol-6-yl, B | Me | I | 100 | $H_2O$ | 332—334 |
| 14 | ,, ,, ,, A | ,, | Cl | 88 | 2N-HCl | 315—320 |

* A = methochloride, B = methiodide, C = ethochloride, D = ethiodide.

† The *dichloride* was obtained directly from the reaction solution by neutralisation with sodium hydrogen carbonate, followed by addition of brine.

| | Found (%) | | | | | | Required (%) | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| No. | C | H | N | Hal | $H_2O$ | Formula | C | H | N | Hal | $H_2O$ |
| 1 | 46·1 | 5·85 | 23·75 | 17·1 | 8·9 | $C_{16}H_{21}Cl_2N_7,2H_2O$ | 45·9 | 6·0 | 23·4 | 16·95 | 8·6 |
| 2 | | | — | | | | | | — | | |
| 3 | — | — | 24·6 | 17·9 | 4·9 | $C_{15}H_{19}Cl_2N_7,H_2O$ | — | — | 24·8 | 17·9 | 4·5 |
| 4 | — | — | 15·5 | 40·4 | 5·5 | $C_{16}H_{25}I_2N_7,2H_2O$ | — | — | 15·6 | 40·4 | 5·7 |
| 5 | — | — | 16·0 | 42·9 | 6·0 | $C_{15}H_{21}I_2N_7,2H_2O$ | — | — | 16·6 | 43·0 | 6·1 |
| 6 | 44·0 | 6·4 | 23·1 | 18·0 | — | $C_{15}H_{21}Cl_2N_7,2H_2O$ | 44·3 | 6·2 | 24·1 | 17·5 | — |
| 7 | — | — | 20·7 | 17·1 | 7·35 | $C_{14}H_{16}Cl_2N_6S,2H_2O$ | — | — | 20·5 | 17·4 | 7·3 |
| 8 | — | — | 13·3 | 40·4 | 10·2 | $C_{16}H_{22}I_2N_6S,3·5H_2O$ | — | — | 13·3 | 40·8 | 10·1 |
| 9 | — | — | 18·6 | 16·0 | 10·6 | $C_{16}H_{22}Cl_2N_6S,2·5H_2O$ | — | — | 18·4 | 15·9 | 10·1 |
| 10 | — | — | 14·2 | 43·0 | 8·7 | $C_{14}H_{18}I_2N_6O,3H_2O$ | — | — | 14·2 | 42·8 | 9·1 |
| 11 | — | — | 24·1 | 20·4 | — | $C_{14}H_{18}Cl_2N_6O$ | — | — | 23·6 | 19·9 | — |
| 12 | — | — | 15·6 | 47·3 | — | $C_{14}H_{18}I_2N_6O$ | — | — | 15·6 | 47·1 | — |
| 13 | — | — | 16·6 | 43·0 | 6·1 | $C_{15}H_{21}I_2N_7,2H_2O$ | — | — | 16·6 | 43·2 | 6·1 |
| 14 | — | — | 23·35 | 17·4 | 8·95 | $C_{15}H_{21}Cl_2N_7,2H_2O$ | — | — | 24·15 | 17·55 | 8·95 |

for 1 hr. The di-iodide, which crystallised on cooling, was converted into the corresponding dichloride by metathesis with silver chloride. The *products* are given in the Table. In some cases equally satisfactory results were obtained if the hydrochloric acid was omitted.

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# 1045. *The Kinetics and Mechanisms of Aromatic Halogen Substitution. Part XI.*[1] *Chlorination of Phenanthrene in Acetic Acid.*

By P. B. D. de la Mare, N. V. Klassen, and R. Koenigsberger.

Phenanthrene and chlorine in acetic acid give 9-chlorophenanthrene as the main product of substitution, but the reaction is accompanied by addition which accounts for more than 40% of the chlorine consumed and gives mainly *cis*-9,10-dichloro-9,10-dihydrophenanthrene, which is much more reactive than the *trans*-isomer with alkali. About 10% of the reaction gives an acetoxychlorodihydrophenanthrene. No evidence of the participation of homolytic processes was obtained. The results are interpreted as further evidence that intermediates of the type $ArHCl_2$, involving halogen with an expanded octet, are important in aromatic substitution.

The discovery [1] that a part of the reaction of chlorine with biphenyl in acetic acid involves addition to the aromatic nucleus led us to consider whether analogous processes would be found for other, chemically related compounds.

Phenanthrene is well known to undergo addition across the 9,10-positions accompanying substitution, and such processes have often [2] been regarded as involving alternative fates of a common intermediate, although for chlorination no detailed study has been made to establish this matter.[3] Sandqvist [4] obtained 9-chlorophenanthrene, m. p. 53°, and a 9,10-dichloro-9,10-dihydrophenanthrene, m. p. 157°, as products of reaction of phenanthrene with one mol. of chlorine. A more detailed study of this reaction comprises the main part of the investigation now reported. A preliminary account has been given elsewhere.[5]

## Experimental

Some of the materials and methods have been described in previous Parts of this series.[6] Phenanthrene was purified by treatment with maleic anhydride.[7] 9-Chlorophenanthrene after repeated recrystallisation from aqueous ethanol had m. p. 53—53·5°. Sandqvist [4] had previously reported the preparation of *trans*-9,10-dichloro-9,10-dihydrophenanthrene, m. p. 156—157°, as a compound of then unknown stereochemistry. We obtained it in very poor yield by treating phenanthrene with chlorine in chloroform. After removal of solvent, the product was dissolved in ethanol, and sodium ethoxide was added until no more was rapidly consumed (lacmoid as indicator). The organic product was precipitated with water, filtered off, and washed several times with light petroleum. It was then recrystallised many times from benzene–light petroleum; the infrared spectrum and chemical behaviour of specimens of m. p. 146° and upwards seemed to be little changed by further purification.

Chlorination in the presence of benzoyl peroxide gave a much purer product. To a solution of phenanthrene (100 g.) and benzoyl peroxide (1 g.) in dry chloroform (200 ml.) was added a slight deficiency of chlorine in chloroform. The solution was left overnight and then shaken with alcoholic sodium ethoxide to remove the *cis*-isomer. The solution was washed with dilute hydrochloric acid and with water, then passed through an alumina column to remove benzoyl peroxide. Most of the chloroform was removed *in vacuo*, and a solid product was precipitated from it by adding light petroleum and cooling the mixture to −78°. The sticky precipitate was washed repeatedly with light petroleum, and the residue was recrystallised several times by cooling, to 5°, a solution in chloroform saturated at 30°. The yield was 6·6 g. The compound decomposes rapidly at or near the m. p. (157°), which was determined by holding

[1] Part X, Beaven, de la Mare, Hassan, Klassen, and Johnson, *J.*, 1961, 2749.
[2] Cf. Price, *J. Amer. Chem. Soc.*, 1936, **58**, 2101; *Chem. Rev.*, 1941, **29**, 37.
[3] Cf. de la Mare and Ridd, "Aromatic Substitution—Nitration and Halogenation," Butterworths Scientific Publ., London, 1959, p. 174.
[4] Sandqvist, *Annalen*, 1918, **417**, 17; Sandqvist and Hagelin, *Ber.*, 1918, **51**, 1515.
[5] de la Mare and Klassen, *Chem. and Ind.*, 1960, 498.
[6] Cf. de la Mare and Hassan, *J.*, 1958, 1519.
[7] Cf. *Org. Synth.*, 1948, **28**, 19; 1954, **34**, 31.

the m. p. block at a steady temperature and inserting a freshly filled capillary. Fusion in less than 1 min. was considered genuine.

In the course of some days the compound decomposed at room temperature, but it could be stored for long periods at −80°; on being heated, it gave hydrogen chloride and 9-chlorophenanthrene.

The stereochemistry is indicated by its relatively small reactivity with alkali, and was proved by partial asymmetric decomposition with brucine—Cristol, Stermitz, and Ramey's method.[8] The dichloride (0·39 g.) was heated in ethanol (30 ml.) with brucine (0·32 g., 0·5 equiv.) at 60° for 6½ days, after which the chloride content of an aliquot part showed that 58% of the dichloride had reacted. The material was dissolved in ether, and brucine was removed by exhaustive extraction with aqueous sulphuric acid. The recovered material, which gave no colour reaction for brucine with concentrated nitric acid, had $\alpha_D$ −0·45° (0·25 g. in 5 ml. of $CHCl_3$; 1 dm. tube). Repeated washing with light petroleum gave a nearly pure specimen of the dichloride, m. p. 154°, $\alpha_D$ −1·67° (0·076 g. in 0·5 ml. of $CHCl_3$; 1 dm. tube). This corresponds to a specific rotation of *ca.* −11°. The recovery of optically active starting material indicates partial asymmetric decomposition of the dichloride, which must therefore be the racemic *trans*-9,10-dichloro-9,10-dihydrophenanthrene.

With ethanolic sodium hydroxide it gave 9-chlorophenanthrene, m. p. without further purification 47° (0·84 g. from 1 g.; 100% yield), identified also by its infrared spectrum. Its rate of dehydrochlorination with sodium ethoxide in ethanol was studied at 58·7°. The initial concentrations of organic compound and sodium ethoxide were 0·0340M and 0·1040M, respectively; 30 ml. portions were titrated with 0·01N-silver nitrate.

| Time (min.) ..... | 0 * | 140 * | 15 | 30 | 45 | 61 | 74 | ∞ |
|---|---|---|---|---|---|---|---|---|
| Titre (ml.) ..... | 1·02 | 1·88 | 4·65 | 8·34 | 11·43 | 14·38 | 16·46 | 103·0 |
| $k_2$ (l. mole$^{-1}$ min.$^{-1}$) †... | — | — | 0·0228 | 0·0244 | 0·0236 | 0·0228 | 0·0220 | — |

* No NaOEt added. † These values correct an error in our preliminary communication.[5]

cis-9,10-*Dichloro*-9,10-*dihydrophenanthrene*.—This compound was present in the crude product obtained by treatment of phenanthrene with chlorine in a wide variety of solvents; it could be detected by its very great reactivity with alkali. Reaction in acetic acid gave material which was shaken with light petroleum (b. p. 40—60°); the *compound* began to separate and, when recrystallised from benzene–light petroleum, had m. p. 101° (Found: C, 67·9; H, 3·8; Cl, 28·5. $C_{14}H_{10}Cl_2$ requires C, 67·5; H, 4·0; Cl, 28·5%). Treatment of this material (0·16 g.) with brucine (0·12 g., 0·5 equiv.) in ethanol (50 ml.) for 19 hr. at room temperature (50% reaction) gave an organic product which within experimental error was optically inactive (0·143 g. in 1 ml. of $CHCl_3$ had a rotation of −0·005°; 1 dm. tube). So this isomer is the internally compensated, (*meso*-)*cis*-9,10-dichloro-9,10-dihydrophenanthrene. Like its isomer, it can be stored at −80° but decomposes slowly at room temperature. It gave 9-chlorophenanthrene in almost quantitative yield when heated or when treated with alcoholic alkali. Its rate of reaction with sodium ethoxide in ethanol was determined. Solutions of *cis*-9,10-dichloro-9,10-dihydrophenanthrene (initially $5·06 \times 10^{-5}$M) and sodium ethoxide (initially $20 \times 10^{-5}$M) were mixed in a 1 cm. silica cell kept (thermostat) at 25°, and readings of the optical density were made at 3000 Å, at which wavelength *cis*-9,10-dichloro-9,10-dihydrophenanthrene has $\varepsilon$ 1600, and 9-chlorophenanthrene has $\varepsilon$ 13,960. The following are readings of optical density as a function of time, interpolated graphically (initial and final values are calculated from the observed spectra of the two compounds):

| Time (min.) ..... | 0 | 2 | 4 | 7 | 13 | 20 | ∞ |
|---|---|---|---|---|---|---|---|
| Optical density ..... | 0·081 | 0·205 | 0·299 | 0·397 | 0·498 | 0·557 | 0·707 |

Values of the integrated second-order velocity-coefficients calculated from these data fall from 560 l. mole$^{-1}$ min.$^{-1}$ at the beginning of the reaction to about 540 l. mole$^{-1}$ min.$^{-1}$ at 50% reaction. The main features of the infrared and ultraviolet spectra of these substances are recorded below.

*Products of Reaction of Phenanthrene with Chlorine in Acetic Acid at* 25°.—(i) *Hydrogen chloride*. After completion of the reaction, hydrogen chloride was determined in reaction mixtures by potentiometric titration with silver nitrate. End-points were stable and were not interfered

[8] Cristol, Stermitz, and Ramey, *J. Amer. Chem. Soc.*, 1956, **74**, 4939.

with by other products. Great care was taken to avoid loss of hydrogen chloride by volatilisation when the sealed vessels were opened. Initial concentrations of chlorine were determined by control measurements. The following are the results:

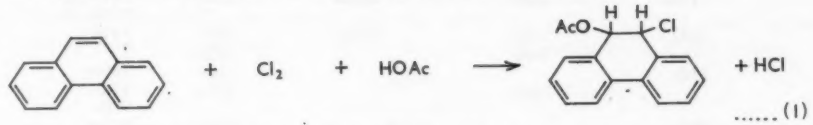
| Init. ArH (M) | Init. $Cl_2$ (M) | Conditions | HCl produced / $Cl_2$ used up | Init. ArH (M) | Init. $Cl_2$ (M) | Conditions | HCl produced / $Cl_2$ used up |
|---|---|---|---|---|---|---|---|
| 0·075 | 0·015 | AcOH, 25° | 0·59 | 0·10 | 0·01 | AcOH, 35° | 0·59 |
| 0·029 | 0·006 | ,, 25 | 0·57 | 0·10 | 0·01 | ,, 45 | 0·59 |
| 0·057 | 0·006 | ,, 25 | 0·58 | 0·07 | 0·04 | ,, 25; added LiCl, 0·02M | 0·58 |
| 0·10 | 0·01 | ,, 15 | 0·58 | | | | |

(ii) *9-Chlorophenanthrene.* 9-Chlorophenanthrene was determined directly in the reaction mixture by the method of isotopic dilution. To a mixture which contained initially 4·50 millimoles of phenanthrene and in which, by titration, it was established that 0·416 millimole of $^{36}Cl$-labelled chlorine had been consumed, inactive 9-chlorophenanthrene (16·68 millimoles) was added. The mixture was then worked up quickly at as low a temperature as possible to avoid decomposition of the dichloride adducts. The molar radioactivity of the diluted 9-chlorophenanthrene after recrystallisation to constant radioactivity showed that 0·1438 millimole of 9-chlorophenanthrene had been produced. On this basis, 0·345 mole of 9-chlorophenanthrene is formed from each mole of chlorine. Repetition gave 0·334 mole.

In a separate experiment, in which 0·414 millimole of $^{36}Cl$-labelled chlorine were used up in reaction with a similar excess of phenanthrene, and the reaction mixture was diluted with 11·59 millimoles of inactive 9-chlorophenanthrene, the bulked diluted organic products were refluxed with an excess of ethanolic alkali for 6 hr. The recovered 9-chlorophenanthrene, now derived in part from the dichloride adducts, had after purification radioactivity corresponding with the formation of 0·3225 millimole (*i.e.*, of 0·78 mole from each mole of chlorine).

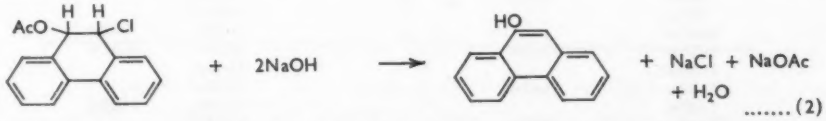
(iii) *Acetoxy-chloride adducts.* The crude product of reaction between chlorine and phenanthrene in acetic acid, isolated by ether extraction and carefully freed from acetic acid, contained oxygen [determined by direct analysis (by A. Bernhardt)] and had a strong infrared absorption band at 1745 $cm.^{-1}$ together with an even stronger band with a main component at 1221 $cm.^{-1}$ and shoulders at *ca.* 1235 and 1205 $cm.^{-1}$. None of these bands appeared in the spectra of the starting material or the other known products; all are characteristic of acetates,[9] and the group of bands in the region of 1220 $cm.^{-1}$ appears to be characteristic of acetates in which the acetoxyl group is not restricted sterically to a single conformation about the C–O bond.[9]

Acetoxy-chloride adducts can be formed by such a reaction as:




..... (1)

Treatment of such adducts with alkali should give acetic acid, hydrogen chloride, and phenanthrol, thus:




..... (2)

Accordingly, the organic product of the reaction of phenanthrene (5 millimoles) with chlorine (2·32 millimoles) in acetic acid (50 ml.) was isolated quantitatively, acetic acid was removed by washing the ether solution with aqueous sodium hydrogen carbonate, and 10 ml. were treated with 10 ml. of 0·0435M-potassium ethoxide in 96% ethanol under reflux for 3 hr. After reaction was complete, aliquot parts were titrated potentiometrically (*a*) with 0·0151N-barium hydroxide, after addition of a known excess of 0·02M-hydrogen chloride, in a current of nitrogen; and (*b*) with silver nitrate. Both these volumetric solutions were standardised against the

[9] Jones and Herling, *J. Amer. Chem. Soc.*, 1956, **78**, 1152; Dauben, Hoerger, and Freeman, *ibid.*, 1952, **74**, 5206.

same standard 0·02M-hydrogen chloride. The results showed that the product liberated 1·62 millimoles (69·8%) of total acid (assumed to be a mixture of hydrogen chloride and acetic acid, as was consistent with the shape of the titration curve) and 1·31 millimoles (56·5%) of chloride ions. 9-Chlorophenanthrene does not liberate chloride under these conditions. From the difference between the results it can be estimated that 0·31 millimole of acetic acid was liberated from the product by alkali; and hence, if a monoacetoxy-monochloride adduct is the main material responsible for the liberation of acetic acid from the product, that 13·4 moles % of chlorine are used up in the reaction to form acetoxychlorodihydrophenanthrene.

The chloride content of the aqueous extract of the reaction mixture was determined by potentiometric titration of an aliquot part against silver nitrate and found to be equivalent to 1·35 millimoles (58·2%). The sum of this figure and the chloride liberated from the reaction product with alkali (1·31 + 1·35 = 2·66 millimoles) exceeds the total chloride (2·32 millimoles) by 0·34 millimole (14·7%). This value ought also be represent an estimate of the amount of acetoxy-chloride adduct calculated as acetoxychlorodihydrophenanthrene. The mean of the two estimates (14%) is used in the following discussion.

The acetoxy-chloride adducts are difficult to isolate in a pure state, as they, like the dichloride adducts, tend to decompose on such chromatographic columns as we have tried.

(iv) *Materials dehydrochlorinated by alkali.* The organic products were carefully freed from hydrogen chloride and acetic acid by washing them in ether solution with aqueous sodium hydrogen carbonate and with water. The residue contained (*a*) material which reacted completely with an excess of alcoholic sodium ethoxide in 10 min. at room temperature, and (*b*) material which reacted much more slowly with alcoholic sodium ethoxide but could be destroyed completely by boiling alcoholic sodium ethoxide in 3 hr. The ratio of rapidly reacting to slowly reacting material, determined by back-titration with acid to the end-point of Bromocresol Green–Methyl Red, was 3·9.

*Infrared Spectra.*—These were recorded for Nujol mulls by using a Grubb-Parsons double-beam spectrophotometer. Some of the results are tabulated.

Infrared absorption bands (cm.$^{-1}$) of phenanthrene and some of its derivatives (range, 650—1350 cm.$^{-1}$).

| Phenanthrene | 9-Chloro-phenanthrene | 9,10-Dichloro-phenanthrene | 9,10-Dichloro-9,10-dihydrophenanthrene *cis*- (m. p. 100°) | 9,10-Dichloro-9,10-dihydrophenanthrene *trans*- (m. p. 157°) |
|---|---|---|---|---|
| | | | | 660m |
| | | | 699m | 704w |
| 713m | 722s | 719m | 712w | 717w,sh |
| | | | | 725m,sh |
| 733s | 744s | 753m | 730s | 732s |
| | 756s | | 740m | |
| 810s | | | 759s | 766m |
| | 846w | | 809m | 774w |
| | | | | 790w |
| 861m | | | 840m | 813w |
| 871m | 858w | | 870sh | 855w |
| | 879m | | 874m | |
| 946m | 935m | | 941w | |
| 971w | | | 951w | |
| 1000w | | | 973w | 973w |
| 1036w | 1042w | | 1026w | 1031w |
| 1089w | | | 1045w | |
| 1138w | 1143w | | 1053w | |
| 1147w | | | 1125w | 1126w |
| 1196w | 1188w | | 1163w | |
| | 1205w | | | 1176w |
| 1242m | 1242w | | 1186m | 1219w |
| 1299m | 1279w | | 1220m | 1230w |
| | 1292w | | 1287w | |
| | | | 1305w | 1312w |

*Ultraviolet Spectra.*—These were determined by using a Unicam S.P. 500 spectrophotometer, 95% ethanol being used as solvent. The spectra of the 9,10-dichloro-9,10-dihydrophenanthrenes are similar in general features to the spectrum of 9,10-dihydrophenanthrene.[10] The

[10] Beaven, Hall, Lesslie, and Turner, *J.*, 1952, 854.

broad absorption band in the region 2700 Å is somewhat reduced in intensity (particularly for the *trans*-compound) and shifted to longer wavelengths. The subsidiary absorption in the region of 3000 Å is reduced in intensity (particularly for the *cis*-compound) and hence is not clearly resolved. No significant absorption was detected in the region 3250—3500 Å, where phenanthrene, 9-chlorophenanthrene, and related compounds have a marked series of weak bands.

Values of the extinction coefficients at maxima and minima according to our measurements are as follows:

9,10-Dihydrophenanthrene, $\varepsilon_{min.}^{2350} = 5000$; $\varepsilon_{max.}^{2640} = 19{,}300$; $\varepsilon_{min.}^{2950} = 4800$; $\varepsilon_{max.}^{3000} = 5050$.

*cis*-9,10-Dichloro-9,10-dihydrophenanthrene, $\varepsilon_{min.}^{2450} = 5200$; $\varepsilon_{max.}^{2700} = 16{,}600$.

*trans*-9,10-Dichloro-9,10-dihydrophenanthrene, $\varepsilon_{min.}^{2500} = 4350$; $\varepsilon_{max.}^{2750} = 12{,}850$.

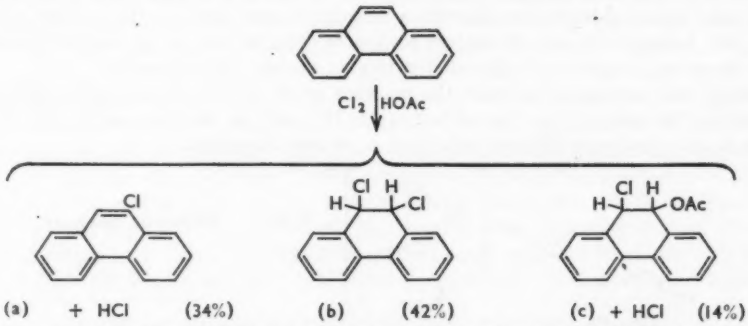
9-Chlorophenanthrene, $\varepsilon_{min.}^{2300} = 10{,}400$; $\varepsilon_{max.}^{2550} = 61{,}200$; $\varepsilon_{min.}^{2850} = 8850$; $\varepsilon_{max.}^{2875} = 11{,}200$; $\varepsilon_{min.}^{2950} = 7700$; $\varepsilon_{max.}^{3000} = 14{,}000$; $\varepsilon_{max.}^{3170} = 298$; $\varepsilon_{max.}^{3270} = 264$; $\varepsilon_{max.}^{3330} = 292$; $\varepsilon_{max.}^{3430} = 214$; $\varepsilon_{max.}^{3500} = 199$.

*Rates of Reaction with Chlorine.*—These were measured in acetic acid (m. p. 16·55°) essentially by conventional methods.[11] Precautions were taken to avoid loss of chlorine by volatility. For phenanthrene, the rate observed ($k_2 = 30 \pm 2$ l. mole$^{-1}$ min.$^{-1}$ at 25° for *ca.* 0·004M-ArH and *ca.* 0·0015M-$Cl_2$) is in good agreement with that recorded by Mason,[12] but in poor agreement with the measurements recorded by Dewar and Mole.[13] We believe that the present value is substantially correct; and we obtained the same value within experimental error when the reaction mixture was illuminated and when the solutions were previously saturated and the vessels flushed either with nitrogen or with oxygen.

9-Chlorophenanthrene, as expected, reacted much more slowly ($k_2 = 0{\cdot}24$ l. mole$^{-1}$ min.$^{-1}$ at 25° for *ca.* 0·04M-ArH, and *ca.* 0·01M-$Cl_2$). The isomeric 9,10-dichloro-9,10-dihydrophenanthrenes reacted still more slowly (*cis*-isomer, $k_2 = 0{\cdot}0015$ l. mole$^{-1}$ min.$^{-1}$; *trans*-isomer, $k_2 = 0{\cdot}0009$ l. mole$^{-1}$ min.$^{-1}$; both at 25°). These two reactions were followed for several days and *ca.* 10% reaction. So, in the time necessary for the reaction of phenanthrene and isolation of the product therefrom, these isomers do not decompose significantly to 9-chlorophenanthrene, which is more reactive than either by a factor of more than 100. This establishes that in the rapid reaction of phenanthrene in acetic acid no significant amount of 9-chlorophenanthrene is formed from either of the isomeric 9,10-dichloro-9,10-dihydrophenanthrenes.

## Discussion

*Detailed Course of the Reaction.*—Cristol, Stermitz, and Ramey[8] found that acenaphthylene with chlorine in a non-polar solvent (where the *trans*-adduct was expected) gave *cis*-dichloroacenaphthene, whereas with benzene iodochloride (where the *cis*-adduct was expected) *trans*-dichloroacenaphthene was obtained. They proved unambiguously the structures of their adducts and commented on the mechanistic implications. The




(a) + HCl (34%) (b) (42%) (c) + HCl (14%)

(a) By isotopic dilution. (b) Total 9-chlorophenanthrene after treatment with alkali, 78%; hence from (a), by difference, 44%. From (HCl liberated) : ($Cl_2$ consumed), 42%. (c) From total acid and total chloride liberated by alkali from organic product.

[11] Cf. de la Mare and Robertson, *J.*, 1943, 279.
[12] Mason, *J.*, 1959, 1233.
[13] Dewar and Mole, *J.*, 1957, 342.

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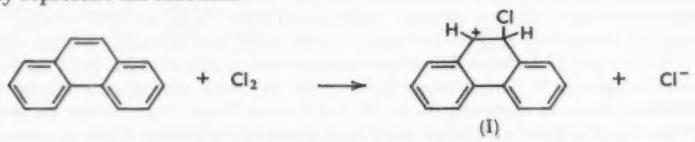
present results for phenanthrene are clearly related to Cristol, Stermitz, and Ramey's findings. For reaction with chlorine in acetic acid in the absence of electrolytes, our results can be summarised by the annexed scheme.

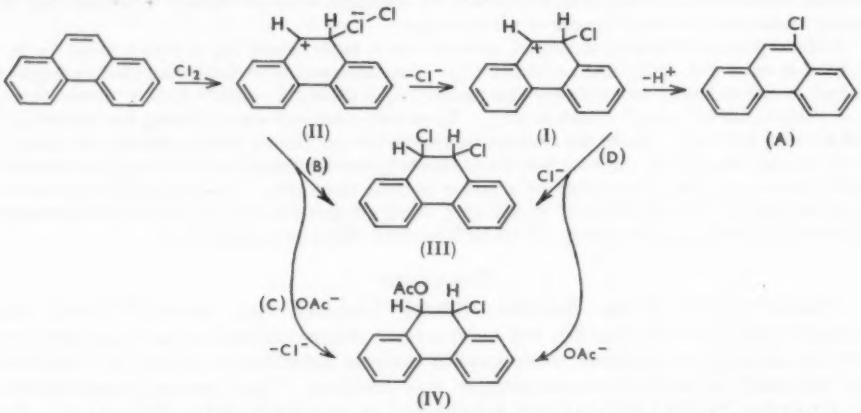
Neither *cis*- nor *trans*-9,10-dichloro-9,10-dihydrophenanthrene decomposes to give significant amounts of 9-chlorophenanthrene under the conditions of the reaction or the working up of the products. Formally, all the indicated products can be considered to be derived from a common carbonium ionic intermediate, (I).

Since, in the presence of added chloride ions, no less hydrogen chloride is produced than in its absence, a scheme involving only the carbonium ionic intermediate cannot adequately represent the reaction.



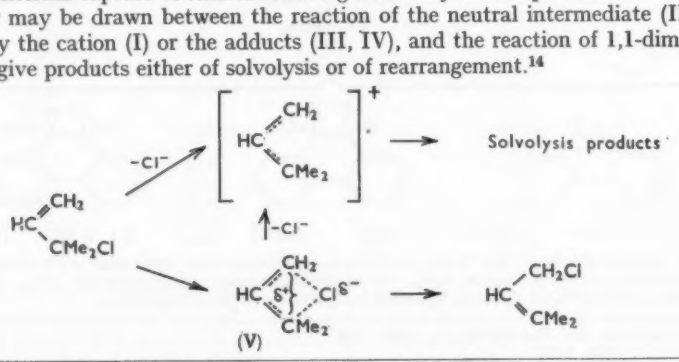

(I)

It is suggested, therefore, that the observations require a more elaborate scheme; the one which we favour is that involving reactions (A)—(D).




Route B is considered to give mainly the *cis*-isomer; it is suggested that it involves partial ionisation of chloride ion, through a transition state which in this solvent resembles an ion-pair, followed [as an alternative to loss of chloride ion giving the carbonium ion, (I)] by the internal capture of chloride ion to give mainly the *cis*-product.

Analogy may be drawn between the reaction of the neutral intermediate (II) to give alternatively the cation (I) or the adducts (III, IV), and the reaction of 1,1-dimethylallyl chloride to give products either of solvolysis or of rearrangement.[14]




[14] Young, Winstein, and Goering, *J. Amer. Chem. Soc.*, 1951, **73**, 1958.

Those who believe that an ion-pair (V) is involved as an intermediate in the true sense (*i.e.*, a minimum which is actually reached by the reacting system in the potential energy surface) in the rearrangement and solvolysis of 1,1-dimethylallyl chloride should be as easily convinced that such an intermediate is the initial product of reaction of the neutral intermediate (II).

The cationic intermediate (I) would be expected by analogy with aliphatic systems [15] to give mainly the *trans*-isomer. In fact, the main products of addition are materials that react rapidly with alkali and must therefore have been formed by *cis*-addition (see below). Kinetic analysis of the reaction mixture is complicated by the fact that it seems that *cis*- and *trans*-isomers both of the dichloride adducts and of the acetoxy-chloride adducts are present. According to our analysis, the extreme assumption being made that all the acetoxy-chloride adduct might be *cis*-, not more than 11% of *trans*-dichloride, and hence not less than 31% of *cis*-dichloride, are produced in the reaction. Investigations leading to further details of the *cis-trans* ratio are in progress.

Route C, leading to acetoxy-chloride adducts, has not been elucidated in detail; it is possible that chloroacetates and dichlorides are in part produced also from the cationic intermediate (I; route D). It is intended to study in more detail the formation of acetoxy-chlorides as a function of the environment, but our analyses suggest that both *cis*- and *trans*-acetoxy-chlorides are formed.

P. W. Robertson and his co-workers [11,16] first emphasised that intermediates, $\overset{+}{\text{Ar}}\text{–}\overset{-}{\text{Hal}}\text{–X}$, involving expanded octets of halogen, were helpful in rationalising kinetic features of the halogenation of aromatic compounds. In the course of the present series, and elsewhere,[17] the possible rôle of such intermediates in determining relative reactivities has been pointed out, and their probable importance in determining the relative effectiveness of reagents Cl–X has been discussed.[18] The present results suggest that the products and stereochemistry of the addition which accompanies substitutions are also in part determined by their intervention in the complicated sequences involved in reaction.

Elsewhere [17] we have stressed the structural analogy between the complexes, $\overset{+}{\text{Ar}}\!\!<^{\text{H}}_{\overset{-}{\text{Cl}}\text{–Cl}}$ (*e.g.*, III), which we regard as concerned in these additions, and the trihalide ions ($\text{Cl}\text{–}\overset{-}{\text{Cl}}\text{–Cl}$). In such complexes the central halogen bears 5 electron-pairs (hybridisation $sp^3d$), which are disposed at the corners of a trigonal bipyramid.[19] The favoured arrangement of the bonded groups in the trihalide ion places these so that the complex is linear. The alternative arrangements, with the Cl–Cl bond at right angles or at 120° to the Ar–Cl bond, illustrated in structure (VI) need, however, to be considered for the neutral complexes if our interpretation of *cis*-addition is correct. It seems likely that these particular electronic arrangements would not be very much less satisfactory than the linear alternative.

*Orientation and Reactivity.*—In the present investigation we have identified positively the conversion of 76% of the reacting chlorine into 9-chlorophenanthrene and 9,10-dichloro-9,10-dihydrophenanthrenes; and of 14% into material in which no chlorine remains in the organic nucleus after treatment of the product with alkali, *i.e.*, into acetoxy-chloride adducts. The amount of other nuclear-substituted phenanthrenes which can have been formed may be as large as 10%, though this figure is subject to the combined uncertainties of isotope-dilution and acetoxyl determination, and could possibly be in error by two or three units %. The conclusion that such isomers are present is consistent with theoretical calculations.

[15] Lucas and Gould, *J. Amer. Chem. Soc.*, 1941, **63**, 2541.
[16] Robertson, Dixon, Goodwin, McDonald, and Scaife, *J.*, 1949, 294; Robertson, *J.*, 1954, 1267.
[17] de la Mare, *J.*, 1949, 2871; "Theoretical Organic Chemistry," Kekulé Symposium, Butterworths Scientific Publ., London, 1959, p. 219.
[18] de la Mare, Hilton, and Varma, *J.*, 1960, 4044.
[19] Gillespie and Nyholm, "Progress in Stereochemistry," ed. Klyne and de la Mare, Butterworths Scientific Publ., London, 1958, Vol. 2, p. 261.

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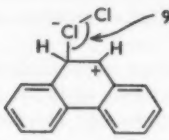
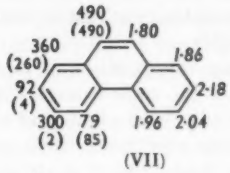
For nitration, Dewar and his co-workers [20] have recorded the partial rate factors indicated in the formula (VII). In this, the italicised numbers are reactivity numbers,




(VI)




(VII)

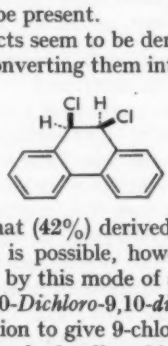
$N_x$, which should, according to simple theory, be related to the partial rate factors through the equation:

$$\log_{10} f_x = \text{Const.}\ (N_0 - N_x) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

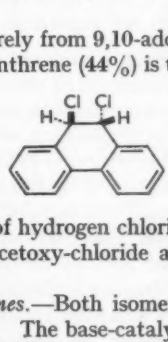
where $N_0$ is the reactivity number (2·31) for benzene. If we assume that the proportionality constant can be obtained from the partial rate factor for the most reactive position, this theory predicts the partial rate factors for nitration given in parentheses; they accord only qualitatively with the experimentally observed values. It has been suggested [21] that the discrepancies arise in part because 1-, 4-, and 9-positions are partly sterically hindered for electrophilic substitution, but analysis of the non-bonded repulsions which might be concerned hardly supports this contention.[3]

A similar analysis can be carried out in part for the chlorination of phenanthrene, by using the rate-ratio, phenanthrene : benzene = $1{\cdot}02 \times 10^6$, established in the present series of investigations.[6] This value accords reasonably with an earlier estimate [3] from the best literature values. If the whole of the observed relative rate of reaction is divided between the various positions according to equation (3), then attack at the 9- and the 1-position should occur in the ratio 84 : 15; less than 1% of reaction should occur at the other nuclear positions. According to this calculation, therefore, up to 15% of 1-chlorophenanthrene might be formed in the chlorination. If the discrepancy between found and calculated values were in the same direction as for nitration, then still more of the 1-chloro-isomer should be present.

The dichloride adducts seem to be derived almost entirely from 9,10-addition, since the amount estimated by converting them into 9-chlorophenanthrene (44%) is the same within




(VIII)




(IX)

experimental error as that (42%) derived from the ratio of hydrogen chloride produced to chlorine consumed. It is possible, however, that the acetoxy-chloride adducts are not produced so exclusively by this mode of addition.

*Chemistry of the* 9,10-*Dichloro*-9,10-*dihydrophenanthrenes*.—Both isomers of this compound undergo elimination to give 9-chlorophenanthrene. The base-catalysed reaction of the *cis*-isomer (VIII) is undoubtedly a bimolecular (*E*2) elimination; it is faster than that for *cis*-dichloroacenaphthene or for any of the isomers of benzene hexachloride.[22] Examination of models shows that the dichloride (VIII) can exist in two equivalent nearly strainless conformations with about 20° between the planes of the aryl groups, in each of which one hydrogen is almost exactly conformationally *trans* to a chlorine atom, as is required for ready bimolecular elimination. This hydrogen atom is relatively accessible; it projects

[20] Bavin and Dewar, *J.*, 1955, 4477; *J.*, 1956, 164; Dewar and Warford, *J.*, 1956, 3570.
[21] Dewar, Mole, and Warford, *J.*, 1956, 3581.
[22] Cristol, Hause, and Meek, *J. Amer. Chem. Soc.*, 1951, **73**, 674; Hughes, Ingold, and Pasternak, *J.*, 1953, 3832.

nearly at right angles to a plane drawn to approximate as nearly as possible to that of both rings.

The reactivity of the *trans*-isomer (IX) seems to be substantially less than that of β-benzene hexachloride,[22] which itself is less than that of *trans*-dichloroacenaphthene.[8] Two nearly strainless conformations are possible for the *trans*-isomer: in neither has either chlorine atom an available conformationally *trans*-hydrogen atom.

We are indebted to Professors E. D. Hughes, F.R.S., Sir Christopher Ingold, F.R.S., Dr. D. M. Hall, and Dr. M. M. Harris for valuable discussions and comment; to Mr. C. Bilby for technical assistance; and to the Council of Bedford College for a Research Fellowship (to R. K.) who is also grateful to J. Lyons and Co. Ltd. for leave of absence.

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## 1046. 1,2-*Quinones from Derivatives of* 2,7-*Dihydroxynaphthalene.*

By F. BELL.

1,2-Naphthaquinones are obtained by the action of nitric acid on derivatives of 2,7-dihydroxynaphthalene. Halogen atoms substituted into certain 2,7-dihydroxy- and 2,7-dimethoxy-naphthalenes are remarkably mobile.

FRIES and SCHIMMELSCHMIDT [1] obtained a number of 1,2-naphthaquinones by oxidation of derivatives of 2-naphthol but the only related observation in the 2,7-dihydroxynaphthalene series is that of Wilson,[2] who obtained in very minute yield the quinone (I) by the oxidation of 1,6-dibromo-2,7-dimethoxynaphthalene with chromium trioxide. It is now found that this compound can be prepared in good yield and in higher purity by use of nitric acid as the oxidising agent.

As dichloro-2,7-dimethoxy- and -dihydroxy-naphthalene are believed [3] to have the halogen atoms in positions 1,6 it was expected that with nitric acid they would yield products analogous to (I), but this was not so. Dichloro-2,7-dimethoxynaphthalene with nitric acid gave a yellow compound, which when heated or crystallised from boiling acetic acid lost nitrosyl chloride and gave a red 1,2-quinone containing only one atom of chlorine. These reactions would be most readily explained if the starting material were 1,8-dichloro-2,7-dimethoxynaphthalene, the yellow intermediate were (II), and the final product (III). Dichloro-2,7-dihydroxynaphthalene behaved similarly in that one chlorine atom was expelled but two nitro-groups simultaneously entered the molecule to give a product most simply formulated as (IV), having regard to the fact [3] that 1,2-naphthaquinone undergoes nitration in position 3. It was then essential to establish the constitution of these dichloro-compounds by synthesis. 1-Chloro-2,7-dimethoxy-8-nitronaphthalene [4] was reduced to the corresponding amine in about 30% yield; rather surprisingly a small amount of 1-chloro-2,7-dimethoxynaphthalene was also produced in this reaction. From the amine there was obtained by the Sandmeyer reaction 1,8-dichloro-2,7-dimethoxynaphthalene, although in very small yield. This was identical with the compound obtained by the dichlorination of 2,7-dimethoxynaphthalene, or by the methylation of dichloro-2,7-dihydroxynaphthalene, and structures (II) and (III) are regarded as confirmed.

When 1-bromo-2,7-dimethoxynaphthalene was chlorinated there was produced a

[1] Fries and Schimmelschmidt, *Annalen*, 1930, **484**, 245.
[2] Wilson, *Tetrahedron*, 1960, **11**, 256.
[3] Zincke and Noack, *Annalen*, 1897, **295**, 1; Fieser and Ames, *J. Amer. Chem. Soc.*, 1927, **49**, 2604.
[4] Bell and Gorrie, *J.*, 1961, 4258.

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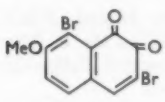
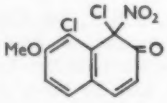
product of somewhat indefinite m. p. Repeated recrystallisation from acetic acid gave material the infrared spectrum of which was essentially identical with that of the product of monobromination of 1-chloro-2,7-dimethoxynaphthalene. This compound gave with nitric acid a naphthaquinone very similar to (I) and regarded as having structure (V). The latter could arise in two ways, (*a*) from 8-bromo-1-chloro-2,7-dimethoxynaphthalene by migration of the bromine atom at some stage in the reaction, or (*b*) directly from



(I)



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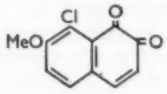

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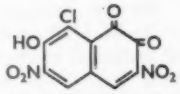

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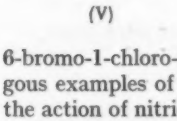

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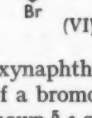

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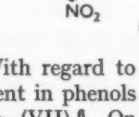

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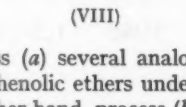

(VIII)

6-bromo-1-chloro-2,7-dimethoxynaphthalene. With regard to process (*a*) several analogous examples of migration of a bromo-substituent in phenols and phenolic ethers under the action of nitric acid are known,[5] *e.g.*, (VI) ⟶ (VII).[6] On the other hand, process (*b*) presupposes a migration of the bromine atom in the course of the chlorination of 1-bromo-2,7-dimethoxynaphthalene, a change which might be regarded as similar to the isomerization of 1,3- to 1,6-dibromo-2,7-dihydroxynaphthalene.[7] The halogen atoms in these naphthalene derivatives are very mobile. Wilson has described the transbromination of 1,6-dibromo-2,7-dihydroxynaphthalene [2] and it is now found that when 1,8-dichloro-2,7-dimethoxynaphthalene is boiled in ethanol containing hydrogen bromide it undergoes conversion into the above bromo-1-chloro-2,7-dimethoxynaphthalene. Since this bromo-1-chloro-compound is not reconverted into the 1,8-dichloro-compound by boiling ethanolic hydrogen chloride and is unaffected by reducing agents (which normally remove α-bromine atoms [7]), the constitution 6-bromo-1-chloro-2,7-dimethoxynaphthalene appears to be indicated.* This provisional conclusion is adopted in the Experimental part.

1-Chloro-2,7-dimethoxy-8-nitronaphthalene with nitric acid suffered loss of halogen to give a 1,2-quinone, probably (VIII). It has already been recorded that 1-bromo-2,7-dimethoxynaphthalene with nitric acid suffers replacement of bromine to give trinitro-2,7-dimethoxynaphthalene.[4]

## Experimental

*Interaction of 1,6-Dibromo-2,7-dimethoxynaphthalene with Nitric Acid.*—Concentrated nitric acid (1 c.c.) in acetic acid (3 c.c.) was added to a warm solution of the compound [7,8] (1 g.) in acetic acid (10 c.c.). In a few minutes the liquid set to a red paste of fine needles of 3,8-dibromo-7-methoxy-1,2-naphthaquinone (I), m. p. 268° (decomp.), unchanged after recrystallisation from a large bulk of acetic acid (Found: C, 38·4; H, 1·7; Br, 46·4; OMe, 9·1. Calc. for $C_{11}H_6Br_2O_3$: C, 38·1; H, 1·7; Br, 46·2; OMe, 9·0%). Wilson [2] gives 244° as the m. p. of this naphthaquinone prepared by the oxidation of 1,6-dibromo-2,7-dimethoxynaphthalene by chromic acid. This experiment was repeated and the product had the m. p. given by Wilson. I am indebted to Dr. D. M. W. Anderson for the report that the infrared spectra of the two samples are essentially identical. The quinone gave a blue-green colour with

* The infrared spectrum closely resembled in pattern that of 1,6-dibromo-2,7-dimethoxynaphthalene and differed markedly from that of 1,8-dichloro-2,7-dimethoxynaphthalene.

[5] Nightingale, *Chem. Rev.*, 1947, **40**, 117.
[6] Sen, *Proc. Nat. Acad. Sci. India*, 1939, **9**, 89; *Chem. Abstr.*, 1941, **35**, 1038.
[7] Cooke, Johnson, and Owen, *Austral. J. Chem.*, 1960, **13**, 256.
[8] Wilson, *Tetrahedron*, 1958, **3**, 236.

concentrated sulphuric acid, and readily condensed with *o*-phenylenediamine in acetic acid to give a *quinoxaline*, which recrystallised from acetic acid in canary-yellow needles, m. p. 215° (Found: C, 48·7; H, 2·2. $C_{17}H_{10}Br_2N_2O$ requires C, 48·8; H, 2·4%).

*Interaction of* 1,8-*Dichloro*-2,7-*dimethoxynaphthalene with Nitric Acid.*—(*a*) Concentrated nitric acid (1 c.c.) in acetic acid (2 c.c.) was added to a hot solution of the compound (1 g.) in acetic acid (10 c.c.). On cooling there separated bright yellow 1,8-*dichloro*-1,2-*dihydro*-7-*methoxy*-1-*nitro*-2-*oxonaphthalene* (II), m. p. 130° (decomp.) (Found: C, 45·7; H, 2·5; Cl, 23·4; OMe, 10·7. $C_{11}H_7Cl_2NO_4$ requires C, 45·8; H, 2·4; Cl, 24·6; OMe, 10·6%). It was easily soluble in chloroform, benzene, and ethyl acetate, but slowly crystallised from solution in hot methanol without change in m. p. Above 130° this compound gave 8-*chloro*-7-*methoxy*-1,2-*naphthaquinone* (III) which formed bright red needles, m. p. 216° (decomp.), from acetic acid (Found: C, 59·3; H, 2·9; Cl, 16·0; OMe, 14·1. $C_{11}H_7ClO_3$ requires C, 59·3; H, 3·1; Cl, 16·0; OMe, 13·9%) and gave a deep green colour with concentrated sulphuric acid.

(*b*) The dimethoxy-compound was introduced slowly into fuming nitric acid; it first gave a brilliant permanganate colour. The resultant solution was poured into water and the red precipitate recrystallised from acetic acid to yield maroon crystals of 8-*chloro*-7-*methoxy*-3(?)-*nitro*-1,2-*naphthaquinone*, m. p. 262° (decomp.) (Found: C, 49·3; H, 2·2. $C_{11}H_6ClNO_5$ requires C, 49·3; H, 2·2%). This compound gives a purple colour with concentrated sulphuric acid and a *quinoxaline*, yellow needles, m. p. 237—240°, with *o*-phenylenediamine in acetic acid (Found: C, 59·7; H, 3·0. $C_{17}H_{10}ClN_3O_3$ requires C, 60·1; H, 2·9%). This quinoxaline gave a deep green colour with concentrated sulphuric acid.

1,8-*Dichloro*-2,7-*dihydroxynaphthalene*.—Sulphuryl chloride (3·5 c.c.) in chloroform was added dropwise to a stirred suspension of 2,7-dihydroxynaphthalene (3·2 g.) in chloroform (20 c.c.). After the vigorous reaction the mixture was warmed on a steam bath and filtered from the main crop (4 g.; m. p. 178—186°). The filtrate, on standing, deposited a further small crop of the same material. One crystallisation from acetic acid raised the m. p. to 187—189°. With methyl sulphate and sodium hydroxide the product readily gave 1,8-dichloro-2,7-dimethoxynaphthalene, m. p. 144° alone or mixed with the product of dichlorination of 2,7-dimethoxynaphthalene (this confirms Wilson's observation [2]). Use of 6 c.c. of sulphuryl chloride in the above preparation led to an almost quantitative yield of 1,1,8-trichloro-1,2-dihydro-7-hydroxy-2-oxonaphthalene, which crystallised from ethanol in large yellow rhombs, m. p. 185° (decomp.).[2]

1,8-Dichloro-2,7-dimethoxynaphthalene was unchanged after being boiled with an ethanolic solution of hydrogen chloride for 2 hr.

*Interaction of* 1,8-*Dichloro*-2,7-*dihydroxynaphthalene with Nitric Acid.*—Fuming nitric acid (2 c.c.) in acetic acid (4 c.c.) was added to the compound (1 g.) in acetic acid (10 c.c.). The mixture became deep red but no crystallisation occurred even on storage. Water precipitated an orange product readily soluble in most solvents. When a solution of it in acetic acid was boiled decomposition set in with evolution of nitrosyl chloride and deposition of red crystals of 8-*chloro*-7-*hydroxy*-(?)3,5-*dinitro*-1,2-*naphthaquinone* (IV), prisms, m. p. 230° (decomp.) (from acetic acid) (Found: C, 40·2; H, 1·0. $C_{10}H_3ClN_2O_7$ requires C, 40·2; H, 1·0%). This quinone becomes black immediately it comes into contact with aqueous solvents. It gives a dichromate colour with concentrated sulphuric acid and with *o*-phenylenediamine in acetic acid a yellow *quinoxaline*, m. p. 262° (Found: C, 52·1; H, 1·6. $C_{16}H_7ClN_4O_5$ requires C, 51·8; H, 1·9%). This quinoxaline gives a dark green colour with concentrated sulphuric acid.

8-*Chloro*-2,7-*dimethoxy*-1-*naphthylamine*.—1-Chloro-2,7-dimethoxy-8-nitronaphthalene [4] (4 g.) was suspended in ethanol (50 c.c., saturated with hydrogen chloride), and stannous chloride (12 g.) was added. The whole was warmed on a steam-bath for 1 hr. during which the liquid became filled with a white precipitate. After cooling, the precipitate was filtered off and decomposed with sodium hydroxide, and the product crystallised from ethanol to yield the *base* as plates, m. p. 104—107° (1·4 g.) (Found: C, 60·0; H, 5·1. $C_{12}H_{13}ClNO_2$ requires C, 60·6; H, 5·1%). The original filtrate, on working up, gave almost black, sticky material from which a small quantity of 1-chloro-2,7-dimethoxynaphthalene was removed by steam.

1,8-*Dichloro*-2,7-*dimethoxynaphthalene*.—The above base (2·8 g.), without further purification, was dissolved in boiling hydrochloric acid (5 c.c. of concentrated acid in 25 c.c. of water), and the solution rapidly cooled to yield the hydrochloride as a paste. To this was added sodium

[2] Bell, Gibson, and Wilson, *J.*, 1956, 2335.

nitrite (0·8 g. in 2 c.c. of water); the whole became very dark. After ½ hr. the liquid was filtered from a considerable black slime, and the golden-yellow filtrate poured into cuprous chloride in hydrochloric acid. A yellow precipitate that was formed proved to be a copper compound, so it was separated and decomposed by boiling dilute hydrochloric acid. The product, repeatedly recrystallised from acetic acid, gave the dichloro-derivative as almost colourless needles, m. p. 144°. Dr. D. M. W. Anderson kindly confirmed that the infrared spectrum of this material was identical with that of the dichlorination product of 2,7-dimethoxynaphthalene.

*6-Bromo-1-chloro-2,7-dimethoxynaphthalene.*—(*a*) Bromine (1 mol.) in chloroform was added to a solution of 1-chloro-2,7-dimethoxynaphthalene in chloroform. Immediate evolution of hydrogen bromide occurred. The mixture was concentrated and then diluted with light petroleum to give an almost quantitative yield of the *6-bromo-derivative*, which crystallised from ethanol in needles, m. p. 128—129° (Found: C, 47·7; H, 3·2. $C_{12}H_{10}O_2BrCl$ requires C, 47·8; H, 3·3%). This compound suffers no appreciable lowering in m. p. on admixture with 1,6-dibromo-2,7-dimethoxynaphthalene, m. p. 128°, supporting the view that the two have identical orientations. (*b*) Hydrobromic acid (15 c.c.; *d* 1·7) was added during 2 hr. to a boiling solution of 1,8-dichloro-2,7-dimethoxynaphthalene (2 g.) in ethanol (50 c.c.). On cooling there separated 0·9 g. of unchanged material. The filtrate on concentration yielded the bromochloro-compound, m. p. and mixed m. p. 128—129°, but considerably depressed on addition of 1,8-dichloro-2,7-dimethoxynaphthalene (Found: C, 47·7; H, 3·3%). (*c*) Sulphuryl chloride (1 mol.) in chloroform was added to a solution of 1-bromo-2,7-dimethoxynaphthalene in chloroform and the mixture concentrated and diluted with light petroleum. The precipitate recrystallised from methanol as needles, m. p. 127° with previous sintering (Found: C, 47·7; H, 3·1%). The infrared spectrum coincided with that of the compound described under (*a*).

In the preparation of 1-bromo-2,7-dimethoxynaphthalene by conducting bromine vapour, in a current of carbon dioxide, into a chloroform solution of 2,7-dimethoxynaphthalene, the leading-in tube became filled with a white solid. This was purified by recrystallisation from pyridine and formed needles, m. p. 193—196° (Found: C, 28·7; H, 1·6; Br, 62·7. Calc. for $C_{12}H_8Br_4O_2$: C, 28·6; H, 1·6; Br, 63·5%) (contrast Cooke, Johnson, and Owen [7]).

*Interaction of 6-Bromo-1-chloro-2,7-dimethoxynaphthalene with Nitric Acid.*—Fuming nitric acid (2 c.c.) in acetic acid was added to a warm solution of the compound (1 g.) in acetic acid (10 c.c.). The dark solution gradually deposited yellow crystals (Found: C, 36·9; H, 1·7%), which decomposed on slight warming or in boiling acetic acid, to give *3-bromo-8-chloro-7-methoxynaphthaquinone* (V), needles (from acetic acid), m. p. 260° (decomp.) (Found: C, 44·2; H, 2·0; Cl, 11·6; Br, 25·9. $C_{11}H_6BrClO_3$ requires C, 43·8; H, 2·0; Cl, 11·8; Br, 26·5. Calc. for $C_{11}H_6BrClO_3,HNO_3$: C, 36·2; H, 1·9%). This compound gives a blue-green colour with concentrated sulphuric acid, and with *o*-phenylenediamine in acetic acid a *quinoxaline*, which recrystallised from acetic acid in canary-yellow needles, m. p. 214—216° (Found: C, 54·4; H, 2·5. $C_{17}H_{10}BrClN_2O$ requires C, 54·6; H, 2·7%).

*Interaction of 1-Chloro-2,7-dimethoxy-8-nitronaphthalene with Nitric Acid.*—The compound [4] (1 g.) was slowly introduced into fuming nitric acid (5 c.c.), and the resultant solution poured in water. The product after recrystallisation from acetic acid formed maroon needles, m. p. 262° (decomp.), of *3(?),8-dinitro-7-methoxy-1,2-naphthaquinone* (VIII) (Found: C, 47·7; H, 2·0; N, 9·9. $C_{11}H_6N_2O_7$ requires C, 47·5; H, 2·2; N, 10·1%). This compound gives a cherry-red colour with concentrated sulphuric acid.

1-Chloro-2,7-dimethoxy-8-nitronaphthalene was unchanged after several hours in hot ethanolic hydrogen bromide.

The author is indebted to Dr. J. W. Minnis for the microanalyses, and to the Carnegie Trust for the Universities of Scotland for a grant.

HERIOT-WATT COLLEGE, EDINBURGH. [*Received, June 15th,* 1961.]

# 1047. *The Polarographic Reduction of Some Heterocyclic Molecules. Part III.* Quinoline Ethiodide.*

By D. J. Casimir, A. J. Harle, and L. E. Lyons.

Quinoline ethiodide is reduced at the dropping mercury electrode over the pH range 2—10, giving a well-defined wave at pH >5 with $E_{\frac{1}{2}}$ — ~0·8 v (*vs.* S.C.E.) for concentrations 2—200 × $10^{-5}$M. This wave corresponds to the addition of one electron to the 1-ethylquinolinium ion. At pH <8 this reduction is followed by a hydrogen discharge which appears as a " peak " on the diffusion current plateau, but at pH <5 tends to merge with the 1-ethylquinolinium ion reduction. Evidence is obtained that the reduction product is adsorbed on the mercury drop and that the final product is a mixture of polymers of the 1-ethylquinolinium radical.

A preliminary polarographic investigation of quinoline showed that the reduction in a buffered supporting electrolyte of low pH, where the quinoline molecule exists predominantly in the protonated form, was difficult to distinguish from the overlying hydrogen discharge. This problem is commonly encountered in the polarographic examination of heterocyclic nitrogen compounds. Quinoline ethiodide was chosen to avoid this difficulty and to allow the reduction mechanism of quinolinium-type ions to be studied over a wide pH range.

Shchennikova and Korshunov [1] investigated the polarography of pyridine, quinoline, and related compounds, including quinoline ethiodide. They studied the reduction of quinoline ethiodide over the pH range 3—10 and observed four reduction waves with pH-independent $E_{\frac{1}{2}}$'s at −0·25, −0·8, −1·2, and −1·7 v. (All potentials are referred to the saturated calomel electrode.) The solutions contained a maximum of 5% of ethanol by volume and buffers contained, appropriately, borax and boric acid, phosphoric, boric, and acetic acids, and sodium hydroxide. No reduction mechanisms were postulated except that for the wave with $E_{\frac{1}{2}}$ −0·8 v which is stated to be possibly due to reduction of the nitrogen–carbon double bond and the formation of a dihydro-compound. The only pH-dependent diffusion current was found in the wave with $E_{\frac{1}{2}}$ at −0·8 v over the pH range 5—7.

The present authors did not observe any reduction wave in the region of −0·25 v and consider the wave at −0·8 v, the diffusion current of which showed little pH-dependence, to be due to the reduction of the 1-ethylquinolinium ion. The two most negative waves reported by the previous workers are similar to a series of anomalous " peaks " observed by us on the diffusion-current plateau when using an aqueous buffered supporting electrolyte. Addition of a relatively large proportion of ethanol has been shown [2] to suppress anomalies in polarographic reduction waves caused by certain types of adsorption at the electrode surface; it was found by the present authors that a 43% concentration of ethanol by weight eliminated all but one of those " peaks " more negative than the quinolinium ion discharge. Thus the polarograms were simplified and it is evident that the remaining peak is not of the type readily removed by the presence of ethanol. All polarographic solutions which were examined contained ethanol at this concentration unless otherwise indicated.

*First Wave.*—Polarographic plots are shown in Figs. 1 and 2. A clear first wave is obtained over the pH range 5—10. In addition, a catalytic hydrogen discharge is obtained at pH <8. At pH <5 this discharge becomes sufficiently positive to prevent study of the first wave.

Fig. 2 indicates that the second part of the first wave is irregular. This irregularity

* Part II, *J.*, 1950, 1575.

[1] Shchennikova and Korshunov, *Zhur. fiz. Khim.*, 1948, **22**, 503.
[2] Kaye and Stonehill, *J.*, 1951, 27, 2638.

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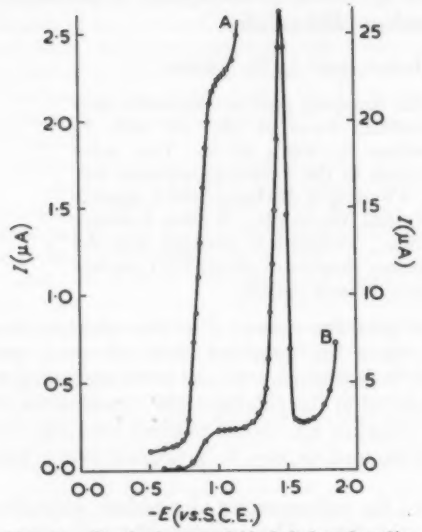


FIG. 1. Typical normal (A, left-hand ordinates) and catalytic (B, right-hand ordinates) polarographic waves of the 1-ethylquinolinium ion. $[Q^+] = 8 \times 10^{-4}$M; pH = 7·54; EtOH concn. = 43%; temp. = 25·0°.

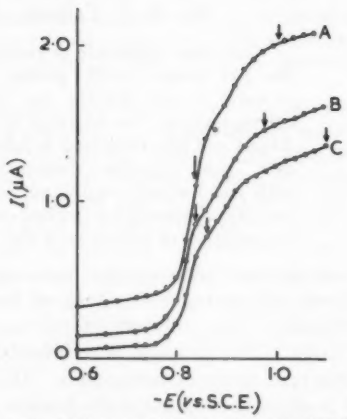


FIG. 2. Influence of ethanol concentration upon first wave. A, 0%; B, 22%; C, 43% of EtOH. Arrows indicate potential range corresponding to abnormal galvanometer oscillations. $[Q^+] = 4 \times 10^{-4}$M; pH = 6·98; temp. = 25·0°.

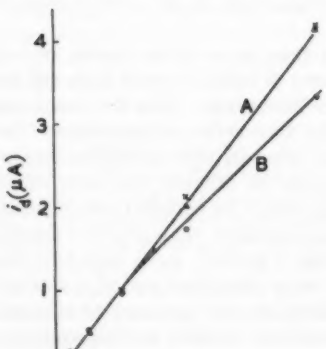


FIG. 3. Dependence of diffusion current, $i_d$, on $[Q^+]$. A, pH = 7·52, 6·98; B, pH = 5·70. EtOH concn. = 43%; temp. = 25·0°.

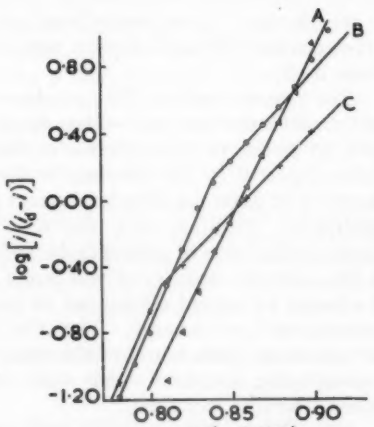


FIG. 4. Effect of $[Q^+]$ upon logarithmic plots. A, $[Q^+] = 8 \times 10^{-5}$M; B, $[Q^+] = 4 \times 10^{-4}$M; C, $[Q^+] = 8 \times 10^{-4}$M. pH = 6·98; EtOH concn. = 43%; temp. = 25·0°.

decreases with increasing pH and at pH 9·5 is difficult to discern. With lower concentrations of the 1-ethylquinolinium ion [Q$^+$], *e.g.*, $8 \times 10^{-5}$M, the irregularity is not present within the pH range examined. We associate the irregularity with adsorption of the reduction product. This is confirmed by the fact that adsorption phenomena were indicated by abnormal galvanometer oscillations during drop growth over the potential ranges shown by arrows in Fig. 2. Abnormalities took the form of a sudden increase in current after drop fall, the current sometimes remaining steady or even decreasing during the remainder of the drop life. Several maxima in the current–drop time relation were sometimes observed. Kaye and Stonehill [2] have reported similar current–time relations with acridines.

Dependence of diffusion current $i_d$ on [Q$^+$] is shown in Fig. 3. The proportionality indicates a diffusion-controlled electrode reaction. A direct relation is observed with [Q$^+$] up to $\sim 5 \times 10^{-4}$M, and with higher [Q$^+$] at pH 7 and above. If the Ilkovic equation holds, the apparent diffusion coefficient at pH 5·7 is reduced by some 40% at high [Q$^+$]. The rate of diffusion of reducible ions to the electrode surface is possibly hindered by electrostatic repulsion arising from an adsorbed product of reduction which is protonated.

The facts that $i_d$ increases 1·8% per °c rise in temperature between 25° and 50° and that $i_d$ is proportional to the square root of the height of the mercury column confirm [3] the view that the wave is diffusion-controlled.

The influence of ethanol concentration is shown in Fig. 2. The decrease in $i_d$ is 30% when the ethanol concentration is increased from 0% to 43%. Similar decreases have been reported with other substances.[2,4] Consequently, by analogy with the diffusion coefficient of quinoline-2- and -4-carboxylic acids,[5] the value of $D^{\frac{1}{2}}$ for the 1-ethylquinolinium ion in 43% ethanol is $2{\cdot}0 \times 10^{-3}$ cm. sec.$^{-\frac{1}{2}}$.

When the value of $D^{\frac{1}{2}}$ so obtained is substituted in the Ilkovic equation, $n$ is found to lie between 0·90 and 1·19 for the conditions studied, indicating the addition of one electron to each cation discharged.

Typical log plots showing variation in slope with [Q$^+$] are given in Fig. 4, revealing a single straight-line log plot only for very low concentrations. When [Q$^+$] $\geqslant 4 \times 10^{-4}$M, the log plot consists of two intersecting straight lines; the plot relating to the first part of the wave is similar in slope to that obtained for the complete wave at low concentrations. The Table gives values for $n$ in the usual expression for a reversible polarographic wave,

$$E = E_{\frac{1}{2}} - (0{\cdot}059/n) \log [i/(i_d - i)],$$

as determined from the slopes of the log plots. These are not integral but have values $n_1$ equal to $1{\cdot}25 \pm 0{\cdot}12$ for the initial section of the wave, and values $n_2$ equal to $0{\cdot}65 \pm 0{\cdot}19$ for the part of the wave at more negative potentials where two distinct log-plot slopes are given.

The best correlation for $n$ values as determined from the Ilkovic equation and log plots occurs, as expected, under conditions where $n = n_1$. For [Q$^+$] $= 8 \times 10^{-5}$M, $n$ (Ilkovic) = 1·19, and $n_1 = 1{\cdot}18 \pm 0{\cdot}06$, indicating the addition of 1 electron per 1-ethylquinolinium ion in the electrode reaction.

Where two slopes are obtained for the log plots, the currents are listed in the Table for the points at which the log plots intersect. The current $i_j$ at the intersection point is constant at a value of $0{\cdot}49 \pm 0{\cdot}05$ μA and is approximately independent of pH, temperature, and ethanol concentration when [Q$^+$] $\geqslant 4 \times 10^{-4}$M. This may be explained by a dependence of the current on the surface area of the electrode. With $m = 0{\cdot}002672$ g. sec.$^{-1}$, $t = 3{\cdot}05$ sec., the maximum surface area attained by the mercury drop is 3·44 mm.$^2$. The number of ions discharged with an average current flow of 0·49 μA over the drop life is $9{\cdot}2 \times 10^{12}$. If all the ions discharged are assumed to remain at the electrode interface,

[3] Gardner and Lyons, *Rev. Pure Appl. Chem.* (*Australia*), 1953, **3**, 137.
[4] Shreve and Markham, *J. Amer. Chem. Soc.*, 1949, **71**, 2993.
[5] Casimir and Lyons, *J.*, 1950, 783.

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Data for logarithmic plots.

| $[Q^+]$ ($10^{-5}$M) | Temp. | pH | [EtOH] (%) | Positive end of wave Slope | $n_1$ | Negative end of wave Slope | $n_2$ | $i_{\frac{1}{2}}$ ($\mu$A) intersection |
|---|---|---|---|---|---|---|---|---|
| 8 | 25° | 5·70 | 43 | 0·047 | 1·25 | — | — | — |
| 8 | 25 | 6·98 | 43 | 0·051 | 1·16 | — | — | — |
| 8 | 25 | 7·51 | 43 | 0·052 | 1·13 | — | — | — |
| 40 | 25 | 5·70 | 43 | 0·051 | 1·16 | 0·11 | 0·536 | 0·54 |
| 40 | 25 | 6·98 | 43 | 0·044 | 1·34 | 0·088 | 0·625 | 0·52 |
| 40 | 50 | 6·98 | 43 | 0·044 | 1·34 | 0·088 | 0·625 | 0·45 |
| 40 | 25 | 7·51 | 43 | 0·041 | 1·44 | 0·082 | 0·720 | 0·54 |
| 40 | 25 | 7·8(?) | 43 | 0·05 | 1·18 | 0·07 | 0·84 | 0·47 |
| 40 | 25 | 6·98 | 0 | 0·032 | 1·90 | 0·088 | 0·625 | 0·53 |
| 40 | 25 | 6·98 | 22 | 0·044 | 1·34 | 0·088 | 0·625 | 0·40 |
| 80 | 25 | 5·70 | 43 | 0·047 | 1·25 | 0·15(?) | — | 0·50 |
| 80 | 25 | 6·98 | 43 | 0·051 | 1·16 | 0·10 | 0·59 | 0·42 |
| 80 | 25 | 7·51 | 43 | 0·042 | 1·40 | 0·066 | 0·90 | — |
| | | | | | | | | Mean 0·49 |

the surface area occupied per reduced ion (if present in a monolayer) can be calculated as 37 sq. Å. This agrees closely with a value of 34 sq. Å obtained for the cross-section of the ion by projection of a scale model with the plane of the aromatic rings perpendicular to the surface, it being reasonable to assume that 1-ethylquinolinium approaches the cathode oriented with the positive centre localized on the nitrogen atom towards the electrode.

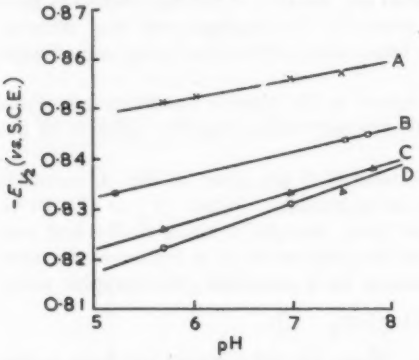


FIG. 5. Dependence of $E_{\frac{1}{2}}$ upon pH. A, $[Q^+] = 8 \times 10^{-5}$M; B, $[Q^+] = 2 \times 10^{-4}$M; C, $[Q^+] = 4 \times 10^{-4}$M; D, $[Q^+] = 8 \times 10^{-4}$M. EtOH concn. = 43%; temp. = 25·0°.

Determination of $E_{\frac{1}{2}}$ by conventional graphical methods, or from log plots, *i.e.*, when $\log i/(i_d - i) = 0$, leads to values which vary over a range of some 40 mv. However, by considering the slope of the log plot for the initial portion of the wave, projected where necessary, values of $E_{\frac{1}{2}}$ are obtained for electrode conditions existing before complete coverage by a monolayer of the reduction product. Fig. 5 shows that $E_{\frac{1}{2}}$ determined graphically depends linearly on pH at any $[Q^+]$. For a given pH, $E_{\frac{1}{2}}$ becomes less negative with increasing $[Q^+]$.

The slopes of the $E_{\frac{1}{2}}$–pH plots are considerably less than those expected for usual participation of hydrogen ion in the electrode reaction. The observed variation is 3·5—6·9 mv/pH unit for $[Q^+]$ between 8 and 80 $\times 10^{-5}$M. Conditions when the reduction is relatively uncomplicated by adsorption occur at high pH and low $[Q^+]$: then $E_{\frac{1}{2}}$ is more negative than −0·86 v (see Table and Fig. 4).

The electrode reaction (A) rather than (B) can therefore be considered to take place in the pH range studied:

$$Q^+ + e^- \longrightarrow \cdot Q_{ads}, \quad \text{(A)}$$

$$Q^+ + e^- + H^+ \longrightarrow \cdot QH^+_{ads}. \quad \text{(B)}$$

Here $\cdot Q_{ads}$ denotes a free radical adsorbed on the mercury surface.

For the electrode reaction taking place at current densities higher than those producing a monolayer at the electrode interface, $E_{\frac{1}{4}}$, determined from the log plots of the more negative section of the wave as indicated previously, becomes more negative with increased $[Q^+]$. It follows that, to discharge the ethylquinolinium ion, more energy is required to transfer an electron through a monolayer (double layer, etc.) of the reduction product at the electrode surface than otherwise. Some irreversibility of the electrode reaction is indicated because $E_{\frac{1}{4}}$ becomes ~0·5 mv more positive per 1°c for all $[Q^+]$ over the temperature range 25—50°.

All the evidence supports electrode mechanism (A), the reduction product being adsorbed in a mono- or multi-layer. However, subsequent dimerization of the reduced cation could occur in the adsorbed layer:

$$\cdot Q_{ads} + \cdot Q_{ads} \longrightarrow (Q\text{–}Q)_{ads}$$

The large-scale reduction of the 1-ethylquinolinium ion by use of a potentiostat similar to that of Lingane and Jones [6] was attempted.[7] An unstable brown-grey amorphous product was obtained from which no single substance could be isolated. Chromatographic investigations indicated the presence of at least ten substances. A variety of substances, corresponding to different degrees of polymerization, was possible from the interaction of the free radicals which were considered to be the initial reduction product.

*Second Discharge.*—Fig. 1 also shows the second discharge which appears, not as a smooth continuation of the initial wave, but as a maximum on the diffusion-current plateau. The addition of maximum-suppressors, *e.g.*, methylcellulose, had little influence, indicating that this is not a maximum of the type normally encountered.

This maximum was observed in the pH range 5—8 and was affected mainly by pH, $[Q^+]$, and buffer capacity. No maximum is present at pH >8·0, and for pH <5·0 the first wave and the buffer discharge merge.

This maximum is due to lowering of hydrogen overvoltage similar to that observed with other heterocyclic nitrogen compounds.[8]

## Experimental

A three-electrode circuit similar to that of Lingane [9] was used with a reproducible liquid junction of negligible potential [10] between cell and saturated calomel reference electrode. Cell and reference electrode were kept (thermostat) at 25·0° ± 0·05° unless otherwise indicated. The polarographic solutions were freed from oxygen by passage of purified hydrogen. Buffer solutions were prepared from "AnalaR" chemicals by addition of the required quantity of concentrated ammonia solution to a solution 0·2M with respect to orthophosphoric acid, acetic acid, and potassium chloride.[11] The pH was recorded by a Doran universal pH-meter.

A Cambridge galvanometer with a curved scale of one metre radius was calibrated by measuring the potential developed across a standard resistance.

Quinoline ethiodide was recrystallised from aqueous ethanol and had m. p. 158—159°.

Capillary characteristics in solutions prepared as above with an applied potential of −1·0 v were $m^{2/3}t^{1/6}$ = 2·57, 2·325, and 2·06 mg.$^{2/3}$ sec.$^{1/6}$ at mercury heads of 56·3, 46·5, and 36·2 cm. respectively.

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[6] Lingane and Jones, *Analyt. Chem.*, 1950, **22**, 1169.
[7] Harle, M.Sc. Thesis, University of Sydney, 1957.
[8] Knobloch, *Coll. Czech. Chem. Comm.*, 1947, **12**, 407; Tompkins and Schmidt, *Univ. California Pub. Physiol.*, 1944, **8**, 229; Stock, *J.*, 1949, 586.
[9] Lingane, *J. Amer. Chem. Soc.*, 1939, **61**, 2099.
[10] Gardner and Diamantis, *Austral. J. Sci.*, 1951, **14**, 23.
[11] Coulson and Cromwell, *J. Amer. Chem. Soc.*, 1952, **74**, 1290.

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## 1048. *The Abstraction of Nitric Oxide from Alkyl Nitrites in the Vapour Phase by Methyl Radicals.*

By (Mrs.) B. Bromberger (née Jest) and L. Phillips.

Methyl radicals, produced by pyrolysis of di-t-butyl peroxide, readily abstract nitric oxide from methyl, ethyl, n-propyl, isopropyl, and t-butyl nitrite in the vapour phase at 160—180°, forming, initially, nitrosomethane and alkoxyl radicals. The latter abstract hydrogen from the nitrosomethane to form the corresponding alcohols. Trimethylhydroxylamine is formed by addition of methyl radicals to nitrosomethane; this is of relevance in the understanding of the inhibition of free-radical reactions by nitric oxide.

The normal reaction of methyl radicals with a hydrogen-containing substrate in vapour-phase photolysis or pyrolysis is hydrogen abstraction to form methane, and reactions of this type have been studied extensively.[1] Until recently very few of the so-called inversion reactions, in which alkyl radicals abstract another atom or group in preference to hydrogen, were known.[2] Abstraction of nitric oxide from s-butyl and 1-ethylpropyl nitrite in the liquid phase by methyl radicals has been reported by Kharasch *et al.*[3] and has been postulated on theoretical grounds by Gray[4] to explain some anomalies in the vapour-phase pyrolysis of t-butyl nitrite. The first experimental evidence for the occurrence of this reaction between methyl radicals and alkyl nitrites in the vapour phase was reported by Jest and Phillips[5] in a preliminary note on the methyl radical–methyl nitrite reaction. Subsequently Gray and Rathbone[6] have demonstrated its occurrence in the liquid phase with t-butyl nitrite. Other recently reported inversion reactions of methyl radicals are abstraction of chlorine atoms from t-butyl hypochlorite in the liquid[7] and the gas phase,[8] and of halogen atoms from alkyl halides.[9]

This paper reports detailed results of studies on the reaction of methyl radicals, from the pyrolysis of di-t-butyl peroxide, with methyl, ethyl, n-propyl, isopropyl, and t-butyl nitrite in the vapour phase at 160—180°.

### Experimental

*Materials.*—Methyl and ethyl nitrite were prepared by simple exchange between the corresponding alcohols and pentyl nitrite. n- and iso-Propyl and t-butyl nitrite were prepared by reaction of nitrous acid with the alcohols in the normal way.[10] After low-temperature fractionation, purity, established by infrared spectroscopy and vapour-phase chromatography, was at least 99·5% except for n-propyl nitrite, which contained about 3% of propionaldehyde. In the last case, mild esterification *via* aluminium nitrite by the method of Chrétrien and Longi[11] failed to effect any improvement. Methyl nitrite was stored as the vapour in blackened flasks; the other nitrites were stored as liquids at −30°.

Di-t-butyl peroxide, supplied by Laporte, was fractionated several times at low temperature; the middle fraction contained no detectable impurities.

*The Reaction.*—Requisite pressures of peroxide and nitrite were measured out individually into a 561 ml. flask, with a mercury–oil manometer (magnification 10).[12] The vapours were

[1] Trotman-Dickenson, "Gas Kinetics," Butterworths Scientific Publ., London, 1955, p. 196.
[2] Ref. 1, p. 237.
[3] Kharasch, Meltzer, and Nudenberg, *J. Org. Chem.*, 1957, **22**, 37.
[4] Gray, *Chem. and Ind.*, 1960, 120.
[5] Jest and Phillips, *Proc. Chem. Soc.*, 1960, 73.
[6] Gray and Rathbone, *Proc. Chem. Soc.*, 1960, 316.
[7] Walling and Jacknow, *J. Amer. Chem. Soc.*, 1960, **82**, 6104.
[8] Phillips, *Proc. Chem. Soc.*, 1961, 338.
[9] Evans, Fox, and Szwarc, *J. Amer. Chem. Soc.*, 1960, **82**, 6414.
[10] *Org. Synth.*, Coll. Vol. II, p. 108.
[11] Chrétrien and Longi, *Compt. rend.*, 1945, **220**, 746.
[12] Drucker, Jimeno, and Kangro, *Z. phys. Chem.*, 1915, *A*, **90**, 513.

frozen individually into a ~150 ml. reaction vessel (previously cleaned with nitric acid and water) fitted with a seal-off construction and breaker tip, and the vessel was sealed whilst the reactants remained frozen. This procedure was necessary in order to achieve partial pressures of peroxide of the order 100 mm. in the reaction vessel at 160—180°, which preliminary work had shown necessary for extensive reaction of methyl radicals with the nitrites. The mixture in the reaction vessel was then preheated to 80° for 10 min. to ensure good mixing and immersed in an " Arochlor " bath which was thermostatically controlled to ±0·1° at 160—180°. At the end of the reaction period, the vessel was rapidly removed from the bath and quenched in cold water. It was then opened *via* the breaker tip under a vacuum, and the products were fractionated through a Leroy still. The first and the second fraction were removed at −193° and −150° and analysed on a Metrovick M.S.3 mass spectrometer. The first fraction contained methane, carbon monoxide, and most of the nitric oxide; the second was mainly ethane with sometimes a little nitric and nitrous oxides and higher hydrocarbons. The liquid products left in the still were removed, measured as vapour, and analysed by infrared spectroscopy and on a Perkin–Elmer model 116 Fraktometer. Doubtful products shown up in the vapour-phase chromatography were frozen out of the hydrogen stream and identified mass-spectrometrically. The stationary phases used in the analysis varied according to the nitrite used and the products obtained. They were usually tetraethylene glycol monomethyl ether for methyl and n-propyl nitrite, tritolyl orthophosphate–polyethylene glycol for ethyl and t-butyl nitrite, and dinonyl phthalate for isopropyl nitrite. The yellowish-brown involatile oils usually left in the reaction vessel were subjected to spot tests for nitroso-compounds, etc., and aqueous extracts examined in a Unicam ultraviolet spectrophotometer.

## Results

On the basis of the results of Raley, Rust, and Vaughan,[13] di-t-butyl peroxide should undergo about 70% decomposition in 30 min. at 160°, and complete decomposition in 30 min. at 180°, according to the equations:

$$Me_3C{\cdot}O{\cdot}O{\cdot}CMe_3 \longrightarrow 2Me_3C{\cdot}O{\cdot} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

$$Me_3C{\cdot}O{\cdot} \longrightarrow Me{\cdot} + Me_2CO \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

$$2Me{\cdot} \longrightarrow C_2H_6 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

Check experiments confirmed this and also showed the presence of small amounts of methane and carbon monoxide, as previously reported. Phillips's data [14] for methyl nitrite show that negligible pyrolysis should occur in 30 min. at 180°; check experiments confirmed this. Similarly Levy's results [15] on ethyl nitrite indicate negligible decomposition in 30 min. at 160° and this was confirmed. The results of Ferguson and Phillips [16] on s-propyl nitrite and of Steacie and Shaw [17] on n-propyl nitrite suggested that about 5% decomposition of each should occur in 30 min. at 160°; this was confirmed.

The analytical results for the reaction of methyl radicals with each of the nitrites are presented separately below. At least four runs were done on each nitrite.

*Methyl Nitrite.*—Results are assembled in Table 1. In addition to the products shown several very small amounts of unidentified products were revealed on chromatography; infrared spectra showed the presence of small amounts of hydrogen cyanide.

Yellowish-brown involatile oily residues having a fishy odour were left in the reaction vessel; these gave the Liebermann nitroso-reaction, and aqueous solutions gave continuous absorption in the 210—250 mμ range, characteristic of formaldoxime. Infrared spectra of the oil at 100—180° suggested the presence of C–N bonds. The chromotropic acid test for formaldehyde gave a positive result, but this is also given by formaldoxime. In order to check whether appreciable amounts of formaldehyde were formed, a run was carried out at 180° in which the products were expanded into an infrared cell maintained at 120° and the infrared spectrum was obtained; at the most a trace (not more than 0·5 mm.) of formaldehyde was detected from the 3·68 μ absorption.

[13] Raley, Rust, and Vaughan, *J. Amer. Chem. Soc.*, 1948, **70**, 88.
[14] Phillips, *J.*, 1961, 3082.
[15] Levy, *J. Amer. Chem. Soc.*, 1956, **78**, 1780.
[16] Ferguson and Phillips, unpublished work.
[17] Steacie and Shaw, *J. Chem. Phys.*, 1935, **3**, 344.

XUM

Trimethylhydroxylamine was identified by freezing out an unknown component, which appeared from its retention volume to have a boiling point of about 30°, from the effluent hydrogen stream from the Fraktometer and determining the mass-spectrometer cracking pattern. Separation of this unknown from the other products was complete except for another unknown which was present in very small amount relative to the amine and could not be separated because of the closeness of the two peaks. The main features of the cracking pattern are shown in Table 2, with that of an authentic sample of trimethylhydroxylamine, prepared

TABLE 1.

Reaction of methyl nitrite with methyl radicals.

| Volatile products (mm. at reaction temp.) | DTBP * 96·8 mm. MeO·NO 128·9 mm. } 30 min. at 180° | DTBP * 101·3 mm. MeO·NO 107·9 mm. } 30 min. at 160° |
|---|---|---|
| $CH_4$ | 15·7 | 10·6 |
| $C_2H_6$ | 22·4 | 10·0 |
| CO | 8·8 | 3·8 |
| NO | 2·6 | 1·2 |
| $N_2O$ | 1·7 | 0 |
| MeO·NO | 61·9 | 63·5 |
| $Me_2CO$ | 196 | 128·6 |
| MeOH | 53·8 | 32·0 |
| DTBP | 0 | 35 |
| $CH_2{:}N{\cdot}OH$ | 14 | NE |
| $Me_2N{\cdot}OMe$ | NE | 9 |
| $Bu^tOH$ | NE | 5 |
| MeO·NO decompd. | 67·0 | 44·4 |

NE = not estimated. * Di-t-butyl peroxide.

TABLE 2.

Some cracking patterns.

| *m/e* | Unknown | $Me_2N{\cdot}OMe$ | *m/e* | Unknown | $Me_2N{\cdot}OMe$ | *m/e* | Unknown | $Me_2N{\cdot}OMe$ |
|---|---|---|---|---|---|---|---|---|
| 14 | 6·1 | 3·7 | 40 | 4·7 | 5·6 | 59 | 8·0 | 0·3 |
| 15 | 38·3 | 32·0 | 41 | 6·4 | 6·9 | 60 | 100·0 | 100·0 |
| 28 | 36·5 | 33·9 | 42 | 55·9 | 56·1 | 61 | 2·7 | 2·2 |
| 29 | 28·0 | 15·6 | 43 | 25·0 | 25·5 | 74 | 3·6 | 3·7 |
| 30 | 18·5 | 11·4 | 44 | 33·3 | 16·7 | 75 | 34·2 | 34·5 |
| 31 | 11·4 | 9·8 | 45 | 12·5 | 15·2 | 76 | 1·3 | 1·3 |
| 39 | 2·4 | 1·7 | | | | | | |

by the method of Jones and Major.[18] Agreement between the major peaks is very good; the differences observed at *m/e* 14, 15, 28, 29, 30, 44, and 59 are due to the presence of the small amount of the other unknown, referred to above, which could not be separated. The spectrum differs considerably from those of other products of the reaction; there is no doubt of the identification as trimethylhydroxylamine. The chromatographic retention volume of synthetic sample was also identical with that found in the reaction products.

Control experiments showed that acetone, formed from the peroxide, had no effect on the straight pyrolysis of methyl nitrite at 180°; neither did small amounts of water vapour which might have been formed in the reaction.

*Ethyl Nitrite.*—Results are reported in Table 3. Several unidentified products were again detected in very small amount. Yellowish-brown involatile oils were left in the reaction vessel; these gave no characteristic Liebermann colours but formaldoxime was indicated by the chromotropic acid test and by ultraviolet spectra of an aqueous extract.

*n-Propyl Nitrite.*—Results are reported in Table 4.

The usual yellowish-brown involatile oil was left in the reaction vessel. No characteristic Liebermann colours were obtained, but traces of formaldoxime were detected as before. After the liquid fraction, condensed at −140° to −150°, had been vaporised and refrozen and revaporised before chromatography, a small amount of a viscous colourless liquid was left; this was probably a product of polymerisation involving n-propyl alcohol and other products.

*Isopropyl Nitrite.*—Results are reported in Table 5.

[18] Jones and Major, *J. Amer. Chem. Soc.*, 1928, **50**, 2742.

TABLE 3.

Reaction of ethyl nitrite with methyl radicals.

| Volatile products (mm. at reaction temp.) | DTBP 113·6 mm. / EtO·NO 108·8 mm. } 30 min. at 160° | DTBP 101·4 mm. / EtO·NO 108·6 mm. } 30 min. at 170° |
|---|---|---|
| $CH_4$ | 12·2 | 18·0 |
| $C_2H_6$ | 10·5 | 16·5 |
| CO | 6·5 | 8·6 |
| NO | 0·8 | 0·6 |
| $N_2O$ | 1·0 | 0·8 |
| EtO·NO | 68 | 52 |
| $Me_2CO$ | 139 | 194 |
| EtOH | 30 | 44 |
| Me·CHO | ~2 | ~3 |
| DTBP | 41 | 0 |
| $Me_2N$·OMe | 8 | N.E. |
| $Bu^tOH$ | 4 | N.E. |
| EtO·NO decompd. | 40·8 | 56·6 |

TABLE 4.

Reaction of n-propyl nitrite with methyl radicals.

| Volatile products (mm. at reaction temp.) | DTBP 90·9 mm. / $Pr^nO$·NO 104·7 mm. } 30 min. at 160° | Volatile products (mm. at reaction temp.) | DTBP 90·9 mm. / $Pr^nO$·NO 104·7 mm. } 30 min. at 160° |
|---|---|---|---|
| $CH_4$ | 15·8 | $Me_2CO$ | 135 |
| $C_2H_6$ | 10·2 | $Pr^nOH$ | 17 |
| CO | 7·7 | DTBP | 20 |
| NO | 1·3 | $Me_2N$·OMe | 9 |
| $N_2O$ | 1·2 | $Bu^tOH$ | 7 |
| $C_3H_8$ | 1·4 | | |
| $Pr^nO$·NO | 62 | PrO·NO decompd. | 42·7 |

TABLE 5.

Reaction of isopropyl nitrite with methyl radicals.

| Volatile products (mm. at reaction temp.) | DTBP 98·1 mm. / $Pr^iO$·NO 109·8 mm. } 30 min. at 160° | Volatile products (mm. at reaction temp.) | DTBP 98·1 mm. / $Pr^iO$·NO 109·8 mm. } 30 min. at 160° |
|---|---|---|---|
| $CH_4$ | 16·5 | $Pr^iOH$ | 23 |
| $C_2H_6$ | 13·0 | DTBP | 25 |
| CO | 5·8 | $Me_2N$·OMe | 8 |
| NO | 0·2 | Me·CHO | 11 |
| $N_2O$ | 0·9 | $Bu^tOH$ | 6 |
| $Pr^iO$·NO | 65 * | | — |
| $Me_2CO$ | 145 | $Pr^iO$·NO decompd. | 34·8 |

* This figure may be slightly high, owing to overlap of a small amount of an unidentified product with the nitrite in the record.

The usual yellowish-brown involatile oil was left in the reaction vessel; traces of formaldoxime were detected in the aqueous washings.

*t-Butyl Nitrite.*—Only a few experiments were done on t-butyl nitrite. The liquid products from a mixture of 84 mm. of di-t-butyl peroxide and 116 mm. of t-butyl nitrite after 30 min. at 160° contained t-butyl nitrite 76 mm., acetone 164 mm., DTBP 17 mm., t-butyl alcohol 29 mm., and trimethylhydroxylamine 10 mm.

## DISCUSSION

The results show that about 40% decomposition of the nitrites studied occurs on reaction with di-t-butyl peroxide at 160° for 30 min.; slightly more reaction occurs as the temperature is raised to 170—180°. Under these conditions simple pyrolysis accounts for losses of only 1—2% with methyl and ethyl nitrite, about 5% with n- and iso-propyl nitrite, and about 8% with t-butyl nitrite.

The gross deficiencies in methyl balances ($CH_3 + 2C_2H_6$), compared with peroxide decomposed suggest a direct reaction between methyl radicals and the nitrites. The normal hydrogen-abstraction reactions

$$Me^{\bullet} + R{\cdot}CH_2O{\cdot}NO \longrightarrow CH_4 + R{\cdot}CHO + NO \quad . . . . . (4)$$
$$Me^{\bullet} + R_2CH{\cdot}O{\cdot}NO \longrightarrow CH_4 + R_2CO + NO \quad . . . . . (5)$$

cannot account for more than a small fraction of the nitrite decomposed because yields of methane are low. Thus, after allowance for the small amounts of methane produced in the pyrolysis of di-t-butyl peroxide itself, the methane produced in 30 min. at 160° in relation to the nitrite decomposed is:

| Nitrite | Me | Et | Pr$^n$ | Pr$^i$ |
|---|---|---|---|---|
| Nitrite decompd. (mm.) ..... | 44·4 | 40·8 | 42·7 | 34·8 |
| $CH_4$ produced (mm.) ..... | 0·8 | 1·2 | 7·0 | 7·0 |

Also no large yields of aldehydes are obtained from the primary nitrites; admittedly they would be expected to react rapidly with methyl radicals but then yields of methane and carbon monoxide would be high.[14, 23]

The large yields of the corresponding alcohols are consistent with the intermediate formation of alkoxyl radicals, and the only logical reaction is abstraction of nitric oxide from the nitrites by methyl radicals to form nitrosomethane, as proposed in an earlier note:[5]

$$Me^{\bullet} + RCH_2{\cdot}O{\cdot}NO \longrightarrow MeNO + R{\cdot}CH_2O^{\bullet} \quad . . . . . (6)$$
$$Me + R_2CH{\cdot}ONO \longrightarrow MeNO + R_2CH{\cdot}O^{\bullet} \quad . . . . . (7)$$

Energetically this reaction is feasible; *e.g.*, for methyl nitrite the enthalpy is −19 kcal./mole.

The occurrence of this type of reaction between methyl radicals (from diacetyl peroxide) and *liquid* s-butyl and 1-ethylpropyl nitrite was first demonstrated by Kharasch *et al.*,[3] and has recently been confirmed by Gray and Rathbone for liquid t-butyl nitrite.[6] These investigators, working at *ca.* 80°, recovered dimeric nitrosomethane in large yields, but it has not been detected in the present work. However, the intermediate formation of nitrosomethane is shown by the detection of small amounts of formaldoxime, which is rapidly formed by isomerisation at 160°,[19] and particularly by the identification of trimethylhydroxylamine which, as reported earlier in a preliminary note,[20] can only arise from addition of methyl radicals to nitrosomethane:

$$2Me^{\bullet} + MeNO \longrightarrow Me_2N{\cdot}OMe \quad . . . . . (8)$$

This reaction is analogous to that proposed by Gingras and Waters[21] to explain the formation of trisubstituted hydroxylamines by reaction of 2-cyano-2-propyl radicals with aromatic nitroso-compounds and with nitric oxide. Hoare[22] has also shown that, in the photolysis of acetone in the presence of small proportions of nitric oxide, up to three methyl radicals can add to one molecule of the latter, but no products were identified.

The large yields of alcohols formed must come from the initially formed alkoxyl radicals by hydrogen abstraction. If this occurred mainly with the parent nitrites, *e.g.*,

$$MeO^{\bullet} + MeO{\cdot}NO \longrightarrow MeOH + CH_2O + NO \quad . . . . . (9)$$

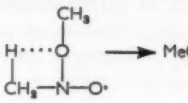
large yields of aldehydes (or of methane plus carbon monoxide as a result of radical attack on the latter[14,23]) would be expected from the primary nitrites. Further, there is evidence[14] that reaction (9) is slow at 180°. Hydrogen abstraction by the alkoxyl radicals from the peroxide or acetone must be slight because yields of acetone are roughly theoretical, and no ethyl methyl ketone was detected. Disproportionation of alkoxyl radicals cannot be

[19] Lüttke, *Z. Elektrochem.*, 1957, **61**, 302.
[20] Phillips, *Proc. Chem. Soc.*, 1961, 204.
[21] Gingras and Waters, *J.*, 1954, 1920.
[22] Hoare, quoted by Batt and Gowenlock, ref. 26 and personal communication.
[23] Toby and Kutschke, *Canad. J. Chem.*, 1959, **37**, 672.

a main source of the alcohols because (*a*) yields of alcohol are too high relative to the amount of nitrite decomposed and (*b*) aldehydes (or their decomposition products) are not detected in large amount, except in the case of isopropyl nitrite where the initially formed isopropoxyl radical breaks down partially into acetaldehyde and a methyl radical.[16]

The alkoxyl radicals must, therefore, abstract hydrogen from nitrosomethane. The absence of mixed ethers (which would arise from addition of methyl and alkoxyl radicals) in the products suggests that free alkoxyl radicals do not exist for long; the probable course of this reaction is rapid addition of alkoxyl radicals to nitrosomethane followed by elimination of the corresponding alcohol, *e.g.*:

$$MeO\cdot + MeNO \longrightarrow Me\cdot N(OMe)O \quad . . . . . (10)$$



$$\longrightarrow MeOH + \cdot CH_2\cdot NO \quad . . . . . (11)$$

Addition of free radicals to nitrosomethane is known to occur easily,[24] and it is confirmed by the formation of trimethylhydroxylamine. The absence of large yields of alcohols and the formation of dimeric nitrosomethane in the liquid-phase work of Kharasch *et al.*[3] and Gray and Rathbone [6] suggest that under their conditions reactions (10) and (11) do not compete with dimerisation of nitrosomethane.

The $\cdot CH_2\cdot NO$ radical formed in reaction (11) probably undergoes further radical addition to give mainly the yellowish-brown involatile oils referred to. Another possibility is the formation of *N*-ethyl-*ON*-dimethylhydroxylamine: $3Me\cdot + \cdot CH_2\cdot NO \longrightarrow MeO\cdot NMeEt$. A further minor unidentified product in the chromatographic analysis of products from the methyl nitrite–di-t-butyl peroxide reaction, which appeared to have a boiling point (judged by its retention volume) of 50—60°, exhibited a mass-spectrometer cracking pattern similar to that which would be expected from *N*-ethyl-*ON*-dimethylhydroxylamine.

Since some of the nitrosomethane initially formed reacts with methyl radicals to form trimethylhydroxylamine, yields of the corresponding alcohols should always be less than the amount of nitrite consumed. Further, the formation of t-butyl alcohol from t-butyl nitrite and the peroxide shows that t-butoxyl radicals abstract hydrogen from nitrosomethane. Some of the t-butoxyl radicals initially formed in pyrolysis of the peroxide should therefore produce t-butyl alcohol on reaction with other alkyl nitrites. This is confirmed by the results although the small yields of t-butyl alcohol show that hydrogen abstraction by these radicals from nitrosomethane is not as easy as with the lower alkoxyl radicals. The relation, $-[RO\cdot NO] = [ROH] + [Bu^tOH] + [Me_2N\cdot OMe]$, should give the nitrosomethane balance; reference to the results shows that this is roughly true.

Gray and Rathbone [6] suggested that these nitric oxide abstraction reactions open a route for radical-chain decomposition in the pyrolysis of nitrites. Thus, at temperatures of at least 200° alkyl radicals are produced from the alkyl nitrites by C–C bond fission of the alkoxyl ra icals initially formed.[25] Any such chains could, however, be terminated by addition of the alkyl radicals produced to the nitrosomethane initially formed, affording trisubstituted hydroxylamines, as shown in this paper. This view is supported by the results given herein of the reaction of methyl radicals with t-butyl nitrite. Methyl radicals are regenerated by breakdown of the t-butoxy-radical formed in the nitric oxide abstraction reaction:

$$Me\cdot + Bu^tO\cdot NO \longrightarrow MeNO + Bu^tO\cdot \quad . . . . . (12)$$

$$Bu^tO\cdot \longrightarrow Me\cdot + Me_2CO \quad . . . . . (2)$$

but the extent of decomposition of the nitrite is about the same as of methyl and ethyl

[24] Gowenlock and Lüttke, *Quart. Rev.*, 1958, **12**, 321.
[25] Adler, Pratt, and Gray, *Chem. and Ind.*, 1955, 1517.

nitrite where no regeneration of methyl radicals occurs after the initial abstraction of nitric oxide.

The formation of trimethylhydroxylamine is of special interest in the inhibition of free-radical vapour-phase reactions by nitric oxide. The importance of further reactions of the nitrosomethane initially formed has recently been emplasised by several authors. Christie [26] suggested the formation of a substituted hydroxylamine by addition of nitric oxide to nitrosomethane, in the photolysis of methyl iodide with an excess of nitric oxide. Hoare [22] has shown that, in the photolysis of acetone–nitric oxide mixtures, methyl radicals and nitric oxide can react in ratios of 3 : 1 and 1 : 3 depending on the relative amounts of each reactant. Batt and Gowenlock [27] isolated a product, which is probably *N*-nitroso-hydroxylamine nitrite, from the reaction of nitrosomethane with nitric oxide at 400°. These observations, together with the identification of trimethylhydroxylamine in the present work, necessitate revision of earlier concepts of inhibition in which one nitric oxide molecule was assumed to remove only one free-radical.*

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* Wojciechowski and Laidler [28] recently suggested that the formation of nitrosoalkanes is of little or no importance in the nitric oxide inhibition of the decomposition of paraffins, and invoke mechanisms depending on formation of HNO. They concede, however, that for other organic molecules such as acetaldehyde and acetone, especially at lower temperatures, formation of nitrosoalkanes is an important termination step.

[26] Christie, *Proc. Roy. Soc.*, 1958, *A*, **249**, 259.
[27] Batt and Gowenlock, *Trans. Faraday Soc.*, 1959, **56**, 682.
[28] Wojciechowski and Laidler, *Canad. J. Chem.*, 1960, **38**, 1027.

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## 1049. *Washburn Numbers in the Methanol–Water–Hydrochloric Acid System at 25°.*

By D. FEAKINS.

A novel e.m.f. method for determining Washburn numbers in the methanol–water–hydrochloric acid system has been investigated. Values of the Washburn number for dilute solutions of hydrochloric acid in 10%, 20·22%, and 43·12% mixtures of methanol by weight with water have been obtained together with values of $\Delta E_m°$ which are differences between the standard e.m.f.s of the cells $H_2|HCl|AgCl–Ag$ and $H_2|HCl|Hg_2Cl_2–Hg$ in water and the mixed solvents.

IF electrodes exist which are reversible to both types of ion yielded by the dissociation of a binary electrolyte, then its thermodynamics may be investigated in any solvent medium by means of the appropriate chemical cell. Thus cells of types (I) and (II)

(I) $H_2|HCl|AgCl–Ag$ [1] $\qquad$ $H_2|HCl|Hg_2Cl_2–Hg$ [2] (II)

have been used to investigate the thermodynamics of hydrochloric acid in a large number of organic solvents and their mixtures with water.

[1] Ives and Janz, " Reference Electrodes," Academic Press, New York, 1961, p. 191.
[2] Ref. 1, p. 143.

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Vol. 1961, page 5308, lines 10/11. *For* *N*-nitrosohydroxylamine *read* *N*-methyl-*N*-nitrosohydroxyl-amine.

In particular, if ${}^{a}E$ = e.m.f. of such a cell in solvent medium a, and ${}^{b}E$ = e.m.f of the same cell in solvent medium b at any arbitrary concentrations, then

$$F({}^{a}E - {}^{b}E) = \Delta G_t,^{*} \quad (1)$$

where $\Delta G_t$ is the free energy of transfer of one mole of the electrolyte from one solvent medium to the other. If the corresponding standard e.m.f.s are ${}^{a}E^{\circ}$ and ${}^{b}E^{\circ}$, then

$$F({}^{a}E^{\circ} - {}^{b}E^{\circ}) = \Delta G_t^{\circ}, \quad (2)$$

the difference in the solvation energy of the electrolyte in the two solvent media.

This quantity may not easily be obtained for many electrolytes because of the lack of suitable reversible electrodes, and this work has not been much extended beyond hydrochloric acid. The important results of Åkerlöf,[3,4] the significance of which has escaped general attention, for alkali chlorides in methanol–water mixtures, were obtained by using amalgam electrodes. It would be desirable, if possible, for these to be confirmed by an independent method.

Grunwald and Bacarella [5] have developed a vapour-pressure method which may be used to determine the rate of free-energy change with respect to solvent composition for any electrolyte in a binary solvent mixture. This valuable method does not appear to have the precision of an e.m.f. method.

This situation prompted the present study of cells with transport. While it has not yet been possible to determine the desired thermodynamic information from cells of this sort, some other results are available which may be thought to justify this preliminary account.

A cell of the type (III), where the solvent medium was an equimolar mixture of

$$\text{Ag–AgCl}|\text{NaCl}(a_2)\vdots\text{NaCl}(a_1)|\text{AgCl–Ag} \quad \text{(III)}$$

methanol and water was used by Butler and Gordon [6] to obtain activity coefficients for the electrolyte *relative to a standard state in that medium.* The equation

$$E = \frac{2RT}{F}\int_{a_1}^{a_2} t_+ \, \mathrm{d} \ln a, \quad (3)\dagger$$

where $a$ is the mean ion activity of the electrolyte and $t_+$ the cation transport number, will be precise if the concentration of the electrolyte is not greatly different in the two half-cells (see below). The required activity coefficients may be found from the e.m.f. measurements if $t_+$ is known as a function of the concentration of the electrolyte over the measured range of concentrations. This type of cell will not give $\Delta G_t$.

Accordingly cells of the type (IV) have been examined in this work. The e.m.f. of

$$\text{Ag–AgCl}\left|\begin{matrix}\text{HCl}(a_2)\\ \text{H}_2\text{O}\end{matrix}\right.\vdots\left.\begin{matrix}\text{HCl}(a_1)\\ \text{CH}_3\text{·OH–H}_2\text{O}\end{matrix}\right|\text{AgCl–Ag} \quad \text{(IV)}$$

such a cell is given by Scatchard [8] as

$$E_- = \frac{2RT}{F}\int_{a_1}^{a_2} t_+^{\mathrm{M}} \, \mathrm{d} \ln a + \frac{RT}{F}\int_{a_{\mathrm{W},1}}^{a_{\mathrm{W},2}} w_{\mathrm{W}} \, \mathrm{d} \ln a_{\mathrm{W}}; \quad (4)$$

$a_1$ and $a_2$ are the mean ion activities of the acid in the mixed solvent and in water, respectively, referred to the same standard state, conveniently the hypothetical standard

* The appropriate algebraic signs of the quantities in equations (1) and (2) and the direction of transfer can be determined by inspection in particular cases.

† The Stockholm convention [7] is used, so that $E$ is the potential of the right-hand electrode with respect to the left-hand electrode.

[3] Åkerlöf, *J. Amer. Chem. Soc.*, 1930, **52**, 2353.
[4] Gurney, "Ionic Processes in Solution," McGraw-Hill Co., New York, 1953, p. 222.
[5] Grunwald and Bacarella, *J. Amer. Chem. Soc.*, 1958, **80**, 3840.
[6] Butler and Gordon, *J. Amer. Chem. Soc.*, 1948, **70**, 2276.
[7] See ref. 1, p. 26.
[8] Scatchard, *J. Amer. Chem. Soc.*, 1953, **75**, 2883.

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state of unit activity *in water* on the molal scale; $a_{W,1}$ and $a_{W,2}$ are the activities of water in the two solvent media. In such a system all transport numbers are measured with respect to one component regarded as stationary. In this case we have chosen to regard the methanol as stationary, so that $t_+^M$ is the cation transport number, and $w_W$ the transport number of water, both with respect to methanol. We adopt Agar's [9] terminology and call $w_W$ the Washburn number of water. We regard $w_W$ as positive if the net transport of water would be towards the negative electrode in an electrolysis. Equation (4) is strictly applicable to cell (III), but only differs significantly from expression (3) when the water activities in each half-cell differ appreciably. For cell (III) this will only arise when the electrolyte concentrations in the two half-cells differ appreciably.

If the water in cell (IV) is regarded as stationary, then

$$E_- = \frac{2RT}{F}\int_{a_1}^{a_2} t_+^W \,\mathrm{d}\ln a + \frac{RT}{F}\int_{a_{M,1}}^{a_{M,2}} w_M \,\mathrm{d}\ln a_M. \qquad (5)$$

In equation (5), $t_+^W$ is the cation transport number and $w_M$ the Washburn number of methanol, both with respect to water; $a_{M,2}$ and $a_{M,1}$ are the activities of methanol in the two solutions.

By considering hypothetical transport number experiments we deduce that

$$t_+^W = t_+^M + \frac{x}{X_W}\cdot w_W, \qquad (6)$$

where $x$ and $X_W$ are respectively the mole fractions of the acid and of water in the solution. In most of the experiments reported $x \ll X_W$, and $w_W$ is small. The two transport numbers then differ inappreciably from each other and from the transport number which would be found from a Hittorf experiment if the relative movement of solvent were neglected. If, for example, the analysis were based on the molality of the solute then, if $t_+^H$ is the transport number so calculated:

$$t_+^H = t_+^M + \frac{xw_W}{X_W}\left[1 + \frac{X_M M_M}{X_W M_W}\right]^{-1}, \qquad (7)$$

where $X_M$ is the mole fraction of methanol, and $M_M$ and $M_W$ are the molecular weights of methanol and water, respectively. In subsequent discussion we put

$$t^M = t^W = t^H = t. \qquad (8)$$

We may also deduce that

$$w_W/w_M = -X_W/X_M. \qquad (9)$$

Consider equation (4). Following Åkerlöf,[3] we may express the mean ion activity of a (1:1) electrolyte in a mixed solvent with respect to the molal standard state in pure water as

$$\ln a_1 = \ln m_1 + \ln \gamma_{S,1} + \ln \gamma_\infty; \qquad (10)$$

$m_1$ is the molality, $\gamma_{S,1}$ the mean ion activity coefficient with respect to a standard state in the mixed solvent, and

$$2RT \ln \gamma_\infty = \Delta G_t^\circ, \qquad (11)$$

the free energy of transfer of the electrolyte between the molal standard states in the two media, water and the mixed solvent. $\gamma_\infty$ is thus unity in pure water.

Combining equations (4) and (11), we have

$$E_- = \frac{2RT}{F}\int_{m_1}^{m_2} t_+ \,\mathrm{d}\ln m + \frac{2RT}{F}\int_{\gamma_{S,1}}^{\gamma_{S,2}} t_+ \,\mathrm{d}\ln \gamma + \frac{2RT}{F}\int_{\gamma_\infty}^{1} t_+ \,\mathrm{d}\ln \gamma_\infty + \frac{RT}{F}\int_{a_{W,1}}^{a_{W,2}} w_W \,\mathrm{d}\ln a_W \qquad (12)$$

[9] Agar, in "The Structure of Electrolytic Solutions," ed. Hamer, John Wiley and Sons, New York, 1959, p. 218.

All the quantities in the first, second, and fourth terms on the right-hand side of (12) are, in principle, measurable, making possible the determination of the third term and hence of $\Delta G_t^\circ$. This method could thus be used for any electrolyte yielding one ion for which a reversible electrode exists.

In practice, there is as yet no independent method of determining Washburn numbers accurately in dilute electrolyte solutions. In the present work, therefore, the procedure has been reversed to determine Washburn numbers in hydrochloric acid solutions, since here the $\Delta G_t^\circ$ term can be independently determined.

The published standard e.m.f.s of the cells (I) and (II) in methanol–water mixtures show poor inter-agreement, so that $\Delta G_t^\circ$ values could not be calculated therefrom with any certainty. This difficulty was overcome by using cell (V) in addition to cell (IV).

$$\mathrm{H_2}\left|\begin{matrix}\mathrm{HCl}(a_2)\\ \mathrm{H_2O}\end{matrix}\right\|\begin{matrix}\mathrm{HCl}(a_1)\\ \mathrm{CH_3{\cdot}OH{-}H_2O}\end{matrix}\left|\mathrm{H_2}\right. \qquad \text{(V)}$$

For cell (V) we have

$$E_+ = \frac{-2RT}{F}\int_{a_1}^{a_2} t_-\,\mathrm{d}\ln a + \frac{RT}{F}\int_{a_{W,1}}^{a_{W,2}} w_W\,\mathrm{d}\ln a_W. \qquad (13)$$

Put

$$\frac{RT}{F}\int_{a_{W,1}}^{a_{W,2}} w_W\,\mathrm{d}\ln a_W = \chi.$$

Examining $\chi$, we find that $a_W$ is a function, not only of the water concentration, but also of the electrolyte concentration, although the effect of the latter may be discounted in sufficiently dilute solutions. $w_W$ may be expected also to be a function of these two variables. In studying the system, the solvent composition was held constant in the mixed solvent half-cell and $\chi$ determined at various electrolyte concentrations. These results were used to obtain $\chi^\circ$, the value of $\chi$ at infinite dilution.

Subtracting equation (13) from equation (4) we obtain:

$$E_- - E_+ = \frac{2RT}{F}\int_{a_1}^{a_2}\mathrm{d}\ln a = E \text{ (say)}. \qquad (15)$$

Examining equation (4), we note that since $t_+$ and $a$ are functions of two variables, the solvent-composition and the electrolyte-concentration, the first term on the left-hand side may not in general be integrated unless the path of the integration is known, that is, unless the composition of the junction between the two half-cells is known at all points. The problem may be greatly simplified if $a_1 = a_2$, or nearly so. For let $x$ be a variable specifying the position of a point in the junction. Let $t_+^{(1)}$ and $t_+^{(2)}$ be the cation transport numbers in the mixed and aqueous media respectively. We may then put

$$t_+ = \tfrac{1}{2}\,(t_+^{(1)} + t_+^{(2)}) + \mathrm{f}(x) = \bar{t}_+ + \mathrm{f}(x). \qquad (16)$$

Then

$$\frac{2RT}{F}\int_{a_1}^{a_2} t_+\,\mathrm{d}\ln a = \frac{2RT}{F}\,\bar{t}_+\int_{a_1}^{a_2}\mathrm{d}\ln a + \frac{2RT}{F}\int_{a_1}^{a_2}\mathrm{f}(x)\,\mathrm{d}\ln a. \qquad (17)$$

The first term on the right-hand side is a perfect differential and may be evaluated directly. Regarding the second term, we know that the variation of the transport number across the junction is small and, if the outer solutions are of equal activity, the variation of activity within the junction should also be small. The probable order of magnitude of this term was calculated by assuming a continuous-mixture junction. When mixtures containing 10% or 20·22% of methanol by weight are employed in the mixed solvent half-cell, this term is negligibly small (<0·01 mv) for solutions of equal activity, because of the very small variation in $t_+$. If a solution containing 43·12% of methanol by weight is employed, this assumption leads to a value of 0·05 mv for the term. No attempt was

made to allow for this term in the final calculations: it was simply added into the experimental error. That this term is very small is borne out in practice by the excellent time-stability of the e.m.f. and its independence of accidental disturbance of the liquid junction.

These quantities were estimated graphically, and the additional uncertainty introduced when $a_1$ is not quite equal to $a_2$ was estimated in the same way. For the present experimental results, this is negligible for all the systems in which 10% and 20·22% methanol solutions are used in the mixed half-cell, and is less than 0·01 mv for all except one of the systems in which 43·12% methanol is used, in which it is less than 0·02 mv.

Combining equations (4), (14), (15), and (17) gives

$$E_- = \bar{t}_+ E + \frac{2RT}{F}\int_{a_1}^{a_2} f(x)\, \mathrm{d} \ln a + \chi, \qquad (18)$$

and neglecting the second term on the right-hand side gives

$$E_- = \bar{t}_+ E + \chi. \qquad (19)$$

In measurements, $a_1$ was adjusted to be approximately equal to $a_2$, either by using Schwab and Ziegenbalg's [10] data, or Harned and Thomas's,[11] or by a short series of experimental trials. (In a few measurements recorded here, the adjustment was not made quite as closely as is practically possible, but it is sufficiently close for the theoretical treatment developed here to be correct.) It will be seen that, if $a_1$ is not very different from $a_2$, then $E$ is small, and it is not necessary to know $\bar{t}_+$ with high precision. With the values of $E$ obtained in the present work, a precision of a few per cent in $\bar{t}_+$ is all that is required. The range of acid concentrations employed in all the solvent media for the determination of $\chi^\circ$ was small, and it has thus been possible to neglect the variation of $t_+$ with acid concentration. The rather larger variation of $t_+$ with methanol concentration has been allowed for by employing for all acid concentrations values interpolated from the measurements of Erdey-Grúz and Majthényi,[12] made by a moving-boundary method at a concentration of 0·025 mole/litre.

A by-product of the measurements is the determination, from equation (15), of the quantity $\Delta G_t^\circ$. This may be used to find the differences in standard e.m.f. of the cells (I) or (II) in water on the one hand and methanol–water mixtures on the other.

## Experimental

E.m.f.s were measured with a Pye Precision Vernier potentiometer in conjunction with a sensitive galvanometer and a standard cell.

The experimental cell differed only in a few features from the one described by Covington and Prue.[13] Two electrode compartments supplied with gas-saturators were connected with a central compartment by side-arms drawn out into jets, and carrying greased taps which enabled the three compartments to be isolated from each other. The three compartments could be detached from each other at greased cone-and-socket joints: this facilitated the cleaning and setting-up of the cell. The aqueous solution filled one electrode compartment and the central compartment, and the solution in the mixed solvent filled the other compartment, the junction being formed therefore at the tip of the side-arm from the latter compartment, with the less dense solution above the denser.

After the electrode compartments had been filled, the cell was clamped firmly in the bath of a thermostat at 25° ± 0·01°, with the isolating taps closed. The aqueous solution was then poured into the central compartment, so forming the liquid junction, and a silver–silver chloride electrode was inserted through a greased ground joint in this compartment, thus sealing it off from the atmosphere. This electrode was only used in the hydrogen electrode measurements.

In dilute solutions of acid, two totally electrolytic electrodes, freshly prepared by Claussen

[10] Schwab and Ziegenbalg, *Z. Elektrochem.*, 1958, **62**, 172.
[11] Harned and Thomas, *J. Amer. Chem. Soc.*, 1935, **57**, 1666; 1936, **58**, 761.
[12] Erdey-Grúz and Majthényi, *Acta Chim. Acad. Sci. Hung.*, 1958, **16**, 417.
[13] Covington and Prue, *J.*, 1955, 3701.

and French's method,[14] were first inserted through ground joints in the electrode compartments. A slow stream of nitrogen was passed through the solutions: this was found to be essential to ensure readings which did not drift with time. A slight further improvement in stability was effected by shielding the electrodes from the light. (The author thanks Dr. R. W. Pittman for this suggestion.) Immediately before a reading was taken, the nitrogen supply was cut off, the electrode compartments were closed to the atmosphere, and the isolating taps were opened. When an e.m.f. constant to ±0·01 mv had been recorded for 1 hr., the electrodes were reversed and the procedure was repeated. The true e.m.f. of the cell, $E_-$, was the mean of the two readings so obtained, and was thus free from the bias potential between the electrodes, which was normally small. The whole procedure needed 4—6 hr. Checks were made in the early stages of the work on the stability of the cell by repeating the whole procedure after 24 hr.; it was rarely found that a drift of more than 0·01 mv had occurred.

The silver–silver chloride electrodes were then removed, a flow of hydrogen was substituted for nitrogen, and two hydrogen electrodes made by the method of Hills and Ives [15] were inserted in each compartment. When fully equilibrated, the two electrodes in a particular compartment normally differed from each other in potential by less than 0·01 mv. To take a measurement, the e.m.f. between each pair of hydrogen electrodes and the central silver–silver chloride electrode was read off in turn, the difference between these readings giving the overall e.m.f. between the hydrogen electrodes, $E_+$. Only one connecting tap was thus open at any time, and the disturbance of the liquid junction which might have occurred if both had been simultaneously open with the hydrogen passing was avoided. Equilibrium (overall e.m.f. constant to ±0·01 mv for 1 hr.) was normally reached in 4—12 hr., and remained constant often for another 24 hr.

In the solutions dilute in acid (<0·1m) there was no reason to believe that the minute amounts of silver chloride dissolved during the silver–silver chloride measurements would adversely affect the hydrogen electrode measurements. The order of measurement described above was thus used for these concentrations, as it was slightly more convenient practically than the reverse order. In the 1m- and 4m-solutions, the hydrogen electrodes behaved irreversibly in solutions saturated with silver chloride, and there was the further problem that the solubility of silver chloride is such in these solutions that it is rapidly stripped from the electrodes unless the solutions are previously saturated with it.

For these measurements, the hydrogen electrode measurements were made first, the middle compartment containing solution previously saturated with silver chloride. Before the silver–silver chloride measurements were made, the solutions in the electrode compartments were replaced by solutions which had previously been saturated with silver chloride.

Conductivity water was obtained from a still of the type described by Stuart and Wormwell.[16] Burrough's " AnalaR "-quality methanol was refluxed for 3 hr. with silver oxide (see ref. 17), dried for one week ($CaSO_4$), and distilled through a 4 ft. vacuum-jacketed column packed with Fenske helices, with rejection of substantial head and tail fractions; it had $n_D^{25}$ 1·3265.

Hopkin and Williams's " AnalaR " hydrochloric acid (the samples used gave a negative test for bromide [18]) was used to prepare a solution of the constant-boiling composition. This was used for all except the 1m- and 4m-solutions, for which the original " AnalaR " acid was employed.

## Discussion

Most of the measurements were made with a 43·12% solution by weight of methanol in water in the " mixed " half-cell, since the effect under examination is larger here than in the 10% and 20·22% mixtures.

Table 1 gives values of $E_-$, $E_+$, $E$, and $\chi$ at various molalities of acid for these three mixtures, together with the cation transport numbers appropriate to each solvent mixture and to water.

[14] Claussen and French, *Trans. Faraday Soc.*, 1955, **51**, 708.
[15] Hills and Ives, *J.*, 1951, 305.
[16] Stuart and Wormwell, *J.*, 1930, 85.
[17] Leighton, Crary, and Schipp, *J. Amer. Chem. Soc.*, 1931, **53**, 3017.
[18] Pinching and Bates, *J. Res. Nat. Bur. Stand.*, 1946, **37**, 311.

TABLE 1.

| Molality of HCl in mixed solution ($m_1$) | Molality of HCl in aq. solution ($m_2$) | $E_-$ (mv) | $E_+$ (mv) (corr. to 760 mm.) | $E$ (mv) | $\chi$ (mv) |
|---|---|---|---|---|---|
| Water: $t_+ = 0{\cdot}827$ | | | | | |
| 10% *Methanol*: $t_+ = 0{\cdot}831$. | | | $\chi^\circ = 0{\cdot}21$ mv | | |
| 0·005143 | 0·005865 | 0·02 | 0·23 | −0·21 | 0·19 |
| 0·01053 | 0·01200 | 0·33 | 0·20 | +0·13 | 0·22 |
| 0·03834 | 0·04401 | 0·43 | 0·19 | +0·24 | 0·23 |
| 20·22% *Methanol*: $t_+ = 0{\cdot}833$. | | | | $\chi^\circ = 0{\cdot}42$ mv | |
| 0·005872 | 0·007609 | 0·23 | 0·54 | −0·31 | 0·49 |
| 0·01005 | 0·01297 | 0·13 | 0·45 | −0·32 | 0·40 |
| 0·01548 | 0·02017 | 0·59 | 0·39 | +0·20 | 0·42 |
| 0·01677 | 0·02184 | 0·57 | 0·38 | +0·19 | 0·41 |
| 0·02039 | 0·02634 | 0·31 | 0·38 | −0·07 | 0·37 |
| 43·12% *Methanol*: $t_+ = 0{\cdot}797$. | | | | $\chi^\circ = 0{\cdot}95$ mv | |
| 0·004898 | 0·007977 | 0·05 | 1·05 | −1·00 | 0·87 |
| 0·006965 | 0·01132 | 0·13 | 1·10 | −0·97 | 0·91 |
| 0·01169 | 0·01909 | 0·50 | 0·98 | −0·48 | 0·89 |
| 0·01992 | 0·03217 | 0·34 | 1·09 | −0·75 | 0·95 |
| 0·03787 | 0·06111 | 0·89 | 0·66 | +0·23 | 0·70 |
| 0·05488 | 0·08606 | 0·11 | 0·94 | −0·83 | 0·78 |
| 0·06718 | 0·1065 | 0·78 | 0·85 | −0·07 | 0·84 |
| 0·1014 | 0·1559 | 0·19 | 0·86 | −0·67 | 0·73 |
| 0·1083 | 0·1607 | −1·08 | 1·02 | −2·10 | 0·63 |
| 0·9136 | 1·2044 | −0·03 | 0·63 | −0·66 | 0·50 |
| 3·936 | 4·506 | −0·35 | 0·51 | −0·86 | 0·34 |

The values of $\chi$ obtained when the " mixed " half-cell contained 43·12% methanol were extrapolated to infinite dilution against the molality of the acid in the mixed solvent, all but the results in the two most concentrated solutions being used. Over the range studied, the variation in $\chi$ is small. A linear dependence of $\chi$ on $m$ was assumed for the extrapolation range: much more accurate results would be required to find the true dependence. While $\chi^\circ$ is 0·95 mv the " smoothed " value of $\chi$ at 0·1m is 0·75 mv, showing a downward trend in $\chi$ with increasing concentration. This is continued, though not in a linear fashion, up to the two highest concentrations used. The variation of $a_W$ with acid concentration in the dilute solutions should be negligible, so that the trend in $\chi$ may reasonably be taken as a trend in $w_W$, but in higher acid concentrations, the expected variations of $a_W$ from its value in dilute solution may be large. Further analysis of these results is at present impossible in the absence of the requisite activity data.

The variation of $\chi$ with $m$ being small for the system involving the 43·12% mixture, the $\chi^\circ$ values for the systems involving 10% and 20·22% mixtures could reasonably be

TABLE 2.

| System ..... | $H_2O$–10% $CH_3{\cdot}OH$ | $H_2O$–20·22% $CH_3{\cdot}OH$ | $H_2O$–43·12% $CH_3{\cdot}OH$ |
|---|---|---|---|
| $w_W$ ..... | 0·14 | 0·13 | 0·13 |

identified with the mean of the results at low concentrations and have been so calculated. The errors on each value of $\chi^\circ$ are about $\pm 10\%$ in each case, including $\pm 0{\cdot}05$ mv in the case of the system involving the 43·12% mixture for the uncertainty in computing the liquid junction potential.

Values of $w_W$ were calculated for each system (the values of $a_W$ found by Butler, Thomson, and Maclennan [19] were used). The values so obtained are of course mean values between those applicable in the particular solvent mixture and in water, and are shown in Table 2. No directly comparable literature values are available, since other determinations refer to concentrated acid solutions, to non-electrolytes other than

[19] Butler, Thomson, and Maclennan, *J.*, 1933, 674.

methanol, and these present in high dilution. Nevertheless the results are of the same order as those found for example by Büchbock [20] ($w_W = 0{\cdot}29$ for 1·1N-HCl in 2·2% resorcinol) by a Hittorf determination, and by Longsworth [21] ($w_W = 0{\cdot}35$, 0·20, and 0·32 for, respectively, 1·5% raffinose in 0·2N- and 1·0N-HCl and 1·5% resorcinol in 1·0N-HCl) by a moving boundary method.

The interpretation of $w_W$ is necessarily speculative. A reasonable first assumption is that the chloride ion does not move large quantities of one non-electrolyte with respect to the other. It is a large ion, the electrostatic field at its surface is weak, and its electrostatic interactions with the solvent molecules are therefore weak also. No significant additional interactions of a quantum-mechanical nature are possible. Any contribution it may make to $w_W$ is further reduced by its small transport number ($t_- \approx 0{\cdot}2$) in the solutions concerned. If we assume then that the contribution made to $w_W$ by the chloride ion is very small, it follows that the hydrogen ion itself also moves only very small amounts of water with respect to methanol or *vice versa*. This is to be expected as the ion is moving largely by its " proton-jump " mechanism, as the high values of $t_+$ in all the solvent media used indicate. Preliminary measurements on alkali chlorides, employing results from cells of type (IV) together with Åkerlöf's results, indicate that for lithium, sodium, and potassium chlorides in 10% methanol the $w_w$ values are of an order of magnitude higher (1·4—1·9).

Rearranging equation (15) with $k = 2{\cdot}3026\boldsymbol{RT}/\boldsymbol{F}$, we obtain

$$E = 2k(\log_{10} a_2 - \log_{10} a_1). \quad (20)$$

From equation (10) we have

$$(E - 2k \log_{10} a_2) = -2k(\log m_1 + \log \gamma_{S,1} + \log \gamma_\infty). \quad (21)$$

Put

$$2k \log \gamma_\infty = \Delta E_m^\circ, \quad (22)$$

which is the difference in the standard molal e.m.f.s of cells (I) or (II) in water and the corresponding cell in the mixed solvent.

Values of $a_2$ can be computed from the molalities and the activity coefficients of hydrochloric acid in aqueous solution. For the latter the unpublished results of Gupta, Hills, and Ives have been used.

Now,

$$\log \gamma_{S,1} = \frac{-A\sqrt{c_1}}{1 + \mathring{a}B\sqrt{c_1}} + bm_1 - \log (1 + 0{\cdot}002M_{xy}m_1), \quad (23)$$

where $A$ and $B$ are the appropriate Debye–Hückel constants, $M_{xy}$ is the mean molecular weight of the solvent, and $\mathring{a}$ has been taken as 4·3. Substituting (23) and (22) in (21) and rearranging gives

$$2k \log_{10} a_2 - E - 2k \log m_1 + \frac{2kA\sqrt{c}}{1 + \mathring{a}B\sqrt{c}} + 2k \log (1 + 0{\cdot}002M_{xy}m_1) = \Delta E_m^\circ + bm_1. \quad (24)$$

Putting all the terms on the left-hand side of equation (24) equal to $\Delta E_m^{\circ\prime}$, we then have

$$\Delta E_m^{\circ\prime} = \Delta E_m^\circ + bm_1. \quad (25)$$

For the 43·12% and 20·22% mixtures, $\Delta E_m^{\circ\prime}$ was plotted against $m_1$ to give straight-line plots which were extrapolated to zero $m_1$ to give $\Delta E_m^\circ$ (see Table 3). The density and dielectric constant data of Schwab and Ziegenbalg [10] were used in these calculations. In the case of the 10% mixture, $\Delta E_m^\circ$ values were determined directly for each concentration by using Harned and Thomas's [11] data for $\gamma_S$ in this mixture, and the value in Table 4 is

[20] Büchbock, *Z. phys. Chem.*, 1906, **55**, 563.
[21] Longsworth, *J. Amer. Chem. Soc.*, 1947, **69**, 1288.

an average of the three values so obtained. All the present $\Delta E_m°$ values are accurate to $\pm 0{\cdot}1$ mv.

TABLE 3.

10% *Methanol*

| | | | |
|---|---|---|---|
| $m_1$ | 0·005143 | 0·01053 | 0·03834 |
| $\Delta E_m°$ (v) | 0·00700 | 0·00668 | 0·00696 |

20·22% *Methanol*

| | | | | | |
|---|---|---|---|---|---|
| $m_1$ | 0·005872 | 0·01005 | 0·01548 | 0·01677 | 0·02039 |
| $\Delta E_m°'$ (v) | 0·01390 | 0·01388 | 0·01397 | 0·01400 | 0·01400 |

43·12% *Methanol*

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| $m_1$ | 0·004898 | 0·006965 | 0·01169 | 0·01992 | 0·03787 | 0·05488 | 0·06718 | 0·1014 | 0·1083 |
| $\Delta E_m°$ (v) | 0·02694 | 0·02700 | 0·02712 | 0·02742 | 0·02740 | 0·02790 | 0·02820 | 0·02871 | 0·02870 |

TABLE 4.

$\Delta E_m°$ values, in volts.

| MeOH concn. | 10% | 20% | 20·22% | 43·12% | 43·3% |
|---|---|---|---|---|---|
| Harned and Thomas [11] | 0·0070 | 0·0136 | — | — | — |
| Austin, Hunt, Johnson, and Parton [22] | — | — | — | — | 0·0285 |
| Oiwa [23] | 0·0069 | 0·0130 | — | 0·0277 | — |
| Schwab and Ziegenbalg [10] | — | — | 0·0135 | 0·0265 | — |
| This work | 0·0069 | — | 0·0138 | 0·0269 | — |

TABLE 5.

Mean molal activity coefficients of hydrochloric acid at rounded concentrations for 43·12% mixtures.

| Molality | 0·005 | 0·01 | 0·02 | 0·05 | 0·1 |
|---|---|---|---|---|---|
| A.H.J.P.[22] (43·3%) | 0·891 | 0·857 | 0·817 | 0·752 | 0·702 |
| Oiwa | 0·893 | 0·859 | 0·815 | 0·745 | 0·700 |
| S.Z. | 0·896 | 0·866 | 0·826 | 0·763 | — |
| This work * | 0·895 | 0·864 | 0·825 | 0·759 | 0·716 |

* For the calculation of $\gamma_{\pm}$, $A = 0{\cdot}774$, $dB = 1{\cdot}625$, $M_{xy} = 22{\cdot}19$, $b = 0{\cdot}147$.

In Table 4, the results are compared with those of Austin, Hunt, Johnson, and Parton,[22] Oiwa,[23] and Harned and Thomas,[11] who have measured standard e.m.f.s of cell (I) in the various solvent media. A value of 0·2224 v, the mean to the nearest 0·1 mv of three independent closely concordant determinations,[24] is used for $E_m°$ in aqueous solution, where a value has not been given by the authors. Also shown are Schwab and Ziegenbalg's [10] results from cell (II); these authors measured $E_m°$ values both in water and in the mixed solvents. All values are quoted to the nearest 0·1 mv; thus differences between 20% and 20·22% solutions, and 43·3% and 43·12% solutions, are negligible. Oiwa's results have been interpolated to give a value for the 43·12% solution. This should be accurate to $\pm 0{\cdot}2$ mv.

The agreement between these results is most unsatisfactory, especially for the 43·12% solution, where the largest difference found, 2 mv, is some ten times the sum of the experimental errors on each determination. The present results agree well with the others for the 10% solution, with all except Oiwa's for the 20·22% mixtures, and are closest to Schwab and Ziegenbalg's for the 43·12% mixtures. This situation would repay further investigation.

Activity coefficients have been calculated in the case of the 43·12% mixture only, and are compared with those of other workers at rounded acid concentrations in Table 5. Oiwa's results are interpolated, and those of Austin, Hunt, Johnson, and Parton relate

[22] Austin, Hunt, Johnson, and Parton, unpublished work; see Parsons, "Handbook of Electrochemical Constants," Butterworths, London, 1959, pp. 32, 74.

[23] Oiwa, *J. Phys. Chem.*, 1956, **60**, 754.

[24] Harned and Ehlers, *J. Amer. Chem. Soc.*, 1932, **54**, 1350; 1933, **55**, 2179; Bates and Bower, *J. Res. Nat. Bur. Stand.*, 1954, **53**, 283; Harned and Paxton, *J. Phys. Chem.*, 1953, **57**, 531.

to a 43·3% mixture. Again, while there is fair agreement between the present results and those of Schwab and Ziegenbalg, the same unsatisfactory spread of results is observed otherwise.

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## 1050. *Polyanion Equilibria in Aqueous Solution. Part I. The Quantitative Analysis of Acidified Tungstate Solutions.*

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A method for the quantitative analysis of acidified tungstate solutions by use of $^{185}W$ and paper chromatography has been developed. The equilibrium between the normal tungstate ion $WO_4^{2-}$ and the paratungstate A ion ($HW_6O_{21}^{5-}$), and the rate of formation of paratungstate B, have been studied.

THE species existing in acidified tungstate solutions have usually been investigated by observing the change in some physicochemical property as acid is progressively added to the solution of the normal tungstate, *e.g.*, by a study of pH,[1] conductivity,[2] temperature,[2b] vapour pressure,[3] Rayleigh turbidity,[4] light absorption,[5] and molecular weight (by cryoscopy,[6] diffusion,[7] or dialysis).[8] These measurements frequently indicate abrupt changes when either seven or nine equivalents of acid have been added to six moles of tungstate ion, $WO_4^{2-}$, corresponding to the formation of the paratungstate A ion $HW_6O_{21}^{5-}$ and the pseudo-metatungstate ion $H_3W_6O_{21}^{3-}$ respectively:

$$7H^+ + 6WO_4^{2-} = HW_6O_{21}^{5-} + 3H_2O$$
$$9H^+ + 6WO_4^{2-} = H_3W_6O_{21}^{3-} + 3H_2O$$

The existence of intermediate ions has also been claimed[9] and the results obtained by different workers do not always agree,[1f] both because of the large number of other species frequently present (*e.g.*, $W_3O_{10}^{2-}$ and paratungstate B) and the difficulty of obtaining solutions in equilibrium. Examination of paratungstate A solutions by absorption

[1] See, *e.g.*, (*a*) Britton, *J.*, 1927, 146; (*b*) Britton and German, *ibid.*, 1930, 1249; (*c*) Brintzinger and Ratanarat, *Z. anorg. Chem.*, 1935, **224**, 97; (*d*) Biehler, *Ann. Chim.* (*France*), 1947, **2**, 489; (*e*) (i) Berkem, *Rev. Fac. Sci. Istanbul*, 1949, **14***A*, 7; *Chem. Abs.*, 1950, **44**, 7179; (*f*) Jander and Kruerke, *Z. anorg. Chem.*, 1951, **265**, 244; (*g*) Pan and Hseu, *Bull. Chem. Soc. Japan*, 1953, **26**, 126; (*h*) Cannon, *J. Inorg. Nuclear Chem.*, 1960, **13**, 269; (*i*) Souchay, *Ann. Chim.* (*France*), 1943, **18**, 61.

[2] See, *e.g.*, (*a*) Dumanski, Buntin, Dijatsch-kovski, and Kniga, *Kolloid Z.*, 1926, **38**, 208; (*b*) Jander and Heukeshoven, *Z. anorg. Chem.*, 1930, **187**, 60; (*c*) Pan, Lin, and Sheng, *Bull. Chem. Soc. Japan*, 1953, **26**, 131; also refs. 1*b*, *d*, *e*, *g*.

[3] Robinson and Sinclair, *J.*, 1934, 642.

[4] Bettinger and Tyree, *J. Amer. Chem. Soc.*, 1957, **79**, 3355.

[5] (*a*) Copaux, *Compt. rend.*, 1913, **156**, 1771; (*b*) Schulz and Spandau, *Z. phys. Chem.*, 1940, **185**, 325; (*c*) Jander and Spandau, *Z. anorg. Chem.*, 1927, **162**, 141; (*d*) Jander, Mojert, and Aden, *ibid.*, 1929, **180**, 129; (*e*) Jander and Jahr, *Kolloid-Beih.*, 1934, **41**, 1; (*f*) Iguchi, *Sci. Papers Coll. Gen. Educ., Univ. Tokyo*, 1957, **7**, 173, 183; also refs. 2*b*, 1*f*, *h*.

[6] Souchay, *Ann. Chim.* (*France*), 1943, **18**, 169; also ref. 2*a*.

[7] (*a*) Herzog, *Z. Elektrochem.*, 1910, **16**, 1003; (*b*) Jahr and Witzmann, *Z. anorg. Chem.*, 1932, **208**, 145; (*c*) Anderson and Saddington, *J.*, 1949, S381; also refs. 5*b*, *c*, *d*, *e*.

[8] (*a*) Brintzinger and Brintzinger, *Z. anorg. Chem.*, 1931, **196**, 55; also ref. 1 (*c*); (*b*) Jander and Spandau, *Z. phys. Chem.*, 1940, *A*, **185**, 325; (*c*) Spitsyn and Pirogova, *Doklady Akad. Nauk S.S.S.R.*, 1957, **115**, 322.

[9] See refs. 1*d*, *f*, *g*, 2*c*.

spectroscopy,[1f] polarography,[10] dialysis,[8d] and chemical reactivity [11] shows that the paratungstate A ion concentration decreases with time owing to the formation of the paratungstate B ion, the exact nature of which is not known.

In 1953, Thilo and Grunze [12] separated the polyphosphate ions by paper chromatography. Murata [13] and Ripan *et al.*[14] have similarly separated the monomeric and the condensed forms of molybdate,[13,14] chromate,[13] vanadate,[13] and tungstate,[13] but no attempt was made to use the method quantitatively. Tungsten has been separated from other ions by ion-exchange at various pH,[15] by paper chromatography with acid solvents,[16] and on a column of 8-hydroxyquinoline [17] at pH 5—6, but in no case was separation of different tungstates noted. The object of this work was to develop a method of estimating polytungstate anions quantitatively by paper chromatography, and to use it to study the aqueous equilibria. The method used is similar to that employed by Ripan and Marcu,[18] but more species were evident in our work, and quantitative analysis for paratungstate A in solutions of different pH was performed with an accuracy of $\pm 5\%$.

## Experimental

*Preparation of Solutions.*—Radioactive sodium tungstate solutions were prepared by addition of a 10% molar excess of sodium hydroxide to "AnalaR" tungstic oxide which had been irradiated in B.E.P.O. at A.E.R.E., Harwell. The solution was filtered before use. All samples of tungstic oxide were allowed to decay for six months to eliminate any short-lived isotopes ($^{187}$W, $^{186}$Re, $^{188}$Re). After this time, conventional absorption methods showed only the presence of a 0·43 Mev β-particle ($^{185}$W, 0·428 Mev), with an additional 2% of detectable γ-activity ($^{181}$W). It may also be calculated that from the irradiation of natural tungsten there will also be produced about 0·001 μc of $^{182}$Ta per mc of $^{185}$W; this was ignored.

*Control of* pH.—The Cambridge pH-meter was standardised with carbonate-free 0·05M-potassium hydrogen phthalate and 0·01M-borax buffers. To obtain reproducible chromatographic behaviour it was essential to exclude carbon dioxide from all solutions. Otherwise, small changes in pH resulted which caused large changes in the composition of the tungstate solutions. Rigid precautions were also necessary to avoid absorption of carbon dioxide whilst the solutions were being pipetted, or transferred on to the paper. All experimental work was therefore carried out in a temperature-controlled glove-box, through which carbon-dioxide free air was maintained at a small positive pressure.

*Chromatographic Technique.*—A 5-μl. sample of the solution was pipetted on to a Whatman No. 1 filter-paper strip, 3 × 30 cm., at 5 cm. from one end. The chromatogram was developed by upward elution at 25° for 4 hr., with carbon dioxide-free 1 : 1 v/v water–ethyl alcohol. The pH of the eluate was not critical provided it was >4.

*Measurement of Activity.*—The dried chromatogram was placed in an automatic scanner which slowly moved it across a 3 mm. slit in an aluminium absorber (1 mm. thick) in front of a Geiger counter with a 7 mg./cm.$^2$ window. The output from the Geiger counter was fed into a ratemeter and a recording milliammeter, so that a continuous record of the radioactivity along the paper strip was obtained.

*Two-dimensional Chromatography.*—Although nearly complete separation of the components of a tungstate solution could often be obtained with unidimensional chromatography, there was usually appreciable tailing between the spots, because the rate of conversion of one species into another on the paper was not negligible. If, after the first unidimensional chromatogram was obtained, a second elution was made at right angles to the first, an estimate of the

[10] Souchay, *Ann. Chim.* (*France*), 1943. **18**, 73.
[11] Jahr, *Naturwiss.*, 1941, **29**, 505; also ref. 10.
[12] Thilo and Grunze, *Sitzungsber. deut. Akad. Wiss., Berlin*, 1953, No. 5.
[13] Murata, *Nippon Kagaku Zasshi*, 1957, **78**, 57, 395; *Chem. Abs.*, 1958, **52**, 7006.
[14] Ripan, Duca, Paladi, Stanescu, and Mayer, *Bull. Soc. chim.* (*France*), 1958, 1507, 1514.
[15] Iguchi, *Sci. Papers Coll. Gen. Educ., Univ. Tokyo*, 1956, **6**, 153; *Chem. Abs.*, 1957, **51**, 9255; Huffman, Oswalt, and Williams, *J. Inorg. Nuclear Chem.*, 1957, **3**, 49; Wilkins, *Talanta*, 1959, **2**, 355.
[16] See, *e.g.*, Kertes and Lederer, *Analyt. Chim. Acta*, 1956, **15**, 543; Majumdar and Mukherjee, *Analyt. Chim. Acta*, 1958, **19**, 480.
[17] Erlenmeyer and Dahn, *Helv. Chim. Acta*, 1939, **22**, 1369.
[18] Ripan and Marcu, *Studii si Cercetari Chim.* (*Fil. Cluj.*), 1959, **10**, 17.

amount of interconversion occurring during the separation could be obtained, and a correction made to the unidimensional chromatograms to obtain an accurate analysis of the mixture.

When the paper was dried after the first chromatographic separation, it was essential for the loaded part of the paper to be kept wet if the properties of the species were to remain unaltered. After the first elution of a piece (20 cm. square) of filter paper, the strip containing the tungsten was kept damp between two Polythene sheets, while the remainder of the paper was dried with an air-dryer. The Polythene sheets were then removed, and the second elution was carried out at right angles to the first. The whole area of the paper was then dried, cut into 1 cm. strips, and scanned. From the data obtained, Figs. 2 and 3 (see below) could be constructed.

*Electrophoresis.*—Sodium tungstate solutions were adjusted with aqueous sodium hydroxide or hydrochloric acid to a pH approximately the same as that of a chosen buffer solution. A sample was pipetted on to a paper-chromatographic strip and wetted with the buffer solution. A current of 6·1 milliamp. was passed along the paper for 6 hr. in an " Eel " electrophoresis apparatus. The movement of the tungsten along the paper was determined by scanning the paper for radioactivity as before (Whatman No. 1 chromatography strip). The field strength was variable (1—10 v/cm.).

It was essential that the ionic environment in acid and alkaline solutions should be closely similar if the relative mobility of the tungstate species in the two cases were to be validly compared. The concentrations of the acetate and ammonium buffers were therefore adjusted so that both had the same conductivity. Thus for $pH = pK_a$, the buffer concentrations were 0·100M for the ammonium buffer and 0·180M for the acetate buffer. Both were also made molar in sodium chloride.

*Analysis.*—Whilst there is no doubt that tungstate polymerisation occurs, an attempt was made to study the charge carried by the polyanion by direct analysis for tungsten and cation on the paper. The paper was divided and extracted with potassium hydroxide, and sodium, tungsten, and chloride were determined. In addition to the radioactive tungsten, radioactive hydrochloric acid ($H^{36}Cl$) was used to acidify the solution in these cases, and the movement of the chloride ion followed chromatographically in the same way as for tungsten. But since the separation of $^{185}W$ and $^{36}Cl$ by instrumental methods is not easy, it was necessary to perform a chemical separation before the radiochlorine contents of the paper sections could be determined. After the extraction with potassium hydroxide and the addition of tungstate and chloride carriers, cobalt tungstate was precipitated [19] at pH 9. It was centrifuged off, washed with water, mounted on a planchette, and radioactively assayed. Addition of fresh tungstate carrier, followed by a similar precipitation, ensured that the $^{185}W$ was completely removed. Silver chloride was then precipitated in acid solution and radioactively assayed in the same way.

Sodium was determined by flame-photometry after removal of the radioactive anions from the original potassium hydroxide extract by anion-exchange. Both the radioactive and the photometer results were standardised by normalising with respect to the total sodium, tungstate, and chloride ion known to be on the paper.

## Results and Discussion

Preliminary results show that above pH 9 most of the tungsten is present as one species (X). Fig. 1a shows a typical chromatogram with a single, well-defined spot at $R_F$ 0·8. At lower pH (Fig. 1b) a second form (Y) appears ($R_F$ 0·4), and the further the acidity increases the more Y increases at the expense of X, until at pH 5·0 the chromatogram is shown as in Fig. 1c. At still lower pH, another species (V) appears at high $R_F$ values; in 0·1N-acid, tungstic oxide is precipitated, causing a well-defined peak (Z′) at $R_F$ 0 (Fig. 1e). Removal of tungstic oxide before chromatographic separation by centrifugation eliminates this component. At all pH, a species Z at $R_F$ 0 (which is not $WO_3$) is found to increase slowly with time as shown in Fig. 1f, g, h.

(a) *Identification of Components.*—This chromatographic behaviour can be interpreted in terms of the generally accepted solution chemistry of tungsten as follows:

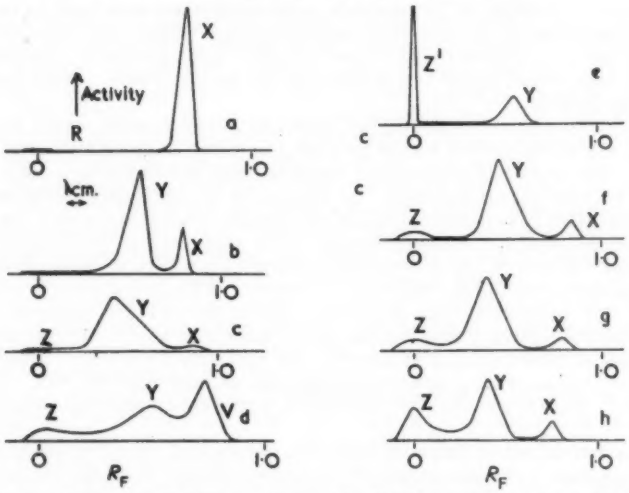
(i) In alkaline solution, the predominant species present (X) is assigned to $WO_4^{2-}$.

[19] Bradhurst, Coller, and Duncan, *J. Inorg. Nuclear Chem.*, 1957, **4**, 379.

This ion, having a relatively low charge and size, would be expected to have a high $R_F$ value. (ii) As the acidity is increased, the first chromatographically separable species (Y) is assigned to the paratungstate A ion $HW_6O_{21}^{5-}$. The decrease in $R_F$ value with increase of size and charge is to be expected by comparison with the chromatographic behaviour of polyphosphates,[20] polymolybdates,[14] and a variety of organic compounds.[21] (iii) Z is produced slowly from $WO_4^{2-}$ (X) and $HW_6O_{21}^{5-}$ (Y) and is taken to be the paratungstate B anion. There will, however, be a contribution from other species having a sufficiently high charge and/or large size to prevent movement along the paper. A chromatogram of freshly dissolved sodium paratungstate ($5Na_2O,12WO_3,28H_2O$) does not exhibit the same chromatographic behaviour as Z. It produces a sharp profile at $R_F = 0$, while Z produces a diffuse band, even in alkaline solutions. (iv) We believe species V to be the pseudo-metatungstate ion $H_3W_6O_{21}^{3-}$.

In some measure these assignments are confirmed by the fact that compounds Y, Z, and V show a blue colour on irradiation with ultraviolet light or sunlight, this fading

FIG. 1. *Radioactivity profiles of* $Na_2WO_4$ *chromatograms.*




(a) pH 9·70, *zero time.* (b) pH 6·77, *zero time.* (c) pH 5·01, *zero time.* (d) pH 2·53, *zero time.*
(e) pH 1·05, *zero time.* (f) pH 6·23, *zero time.* (g) pH 6·23, 2·2 *days.* (h) pH 6·23, 6·5 *days.*

after 3 hours in the dark. This reaction is due to reduction of $W^{VI}$ to lower-valency states [22] and has only been reported when acidified tungstate solutions are absorbed on paper.[1d] Since X is the only form not to show this reaction, it must be $WO_4^{2-}$, and the other peaks must be due to polymerisation.

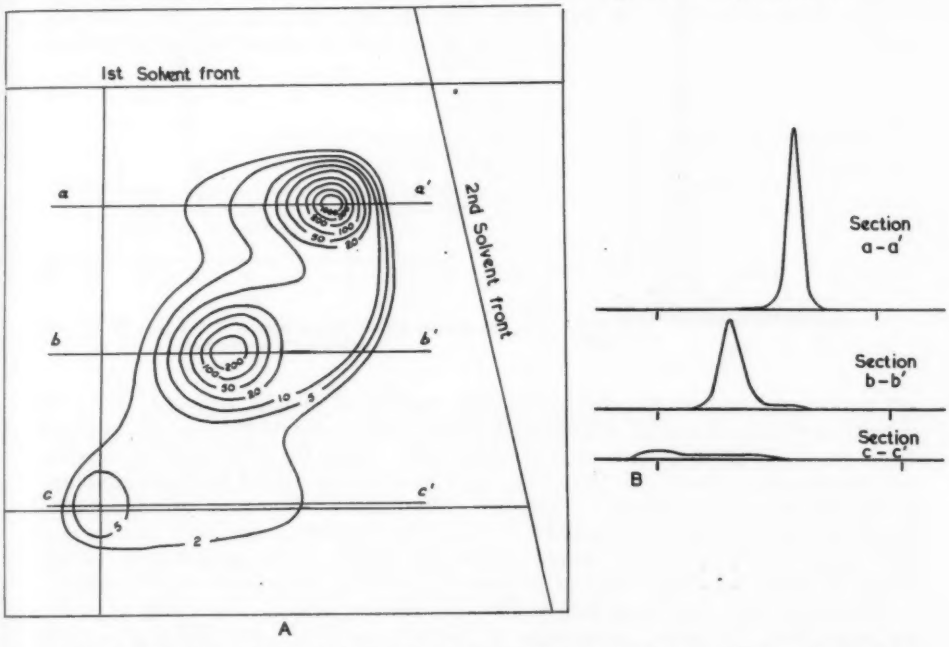
(b) *Interconversion of Tungstates.*—The separation procedure was developed as a method of studying the equilibrium between $WO_4^{2-}$ and $HW_6O_{21}^{5-}$, which is complete in solution within 1—2 min. Nevertheless, the species can be separated by paper chromatography with very little interconversion during the process. For quantitative work, however, it is necessary that the degree of interconversion be known, and this was determined by two-dimensional chromatography. Fig. 2 shows a typical result from the two-dimensional chromatogram of a solution containing X ($WO_4^{2-}$), Y ($HW_6O_{21}^{5-}$),

[20] Thilo and Feldman, *Z. anorg. Chem.*, 1959, **298**, 316.
[21] Bate-Smith and Westall, *Biochim. Biophys. Acta*, 1950, **4**, 429.
[22] Bolliger and Hinks, *Austral. J. Sci.*, 1948, **11**, 60; Bolliger, *ibid.*, 1946, **9**, 166.

and Z (paratungstate B). By considering sections through the activity contours aa′, bb′, and cc′ respectively, it can be seen that 1—2% of X ($WO_4^{2-}$) tails behind, 4—5% of Y ($HW_6O_{21}^{5-}$) appears as X, and Z (paratungstate B) produces a broad band along the paper as far as the front of Y. By means of these data the one-dimensional chromatograms can be corrected so that an accurate estimate of the quantity of each species present in the original solution may be made (see Fig. 3 for a typical case). The combined error from the statistics of counting, and in estimating the areas under the profiles, was less than ±5%.

The interconversion between X ($WO_4^{2-}$) and Y ($HW_6O_{21}^{5-}$) is not unexpected, since equilibrium between the paratungstate A ion and the normal tungstate ion is reached

FIG. 2. (A) *Two dimensional chromatogram: contours are successively* 2, 5, 10, 50, 100, 200, 500, *and* 1000 *counts per min. per* 0·08 *cm.*². (B) *Activity profiles through sections* aa′, bb′, *and* cc′.




rapidly in solution. Nevertheless, effective separation can be obtained. Polymolybdates [14] and cadmium ammines [23] are other examples of chromatographic separation of the components of a rapidly established solution equilibrium.

For two species to be chromatographically separable, their rates of interconversion must be considerably retarded. One of the factors which affects the relative rates of reaction on a chromatogram, compared with those in solution, is the diclectric constant. The change in the rate constant, $k$, for the reaction between ions of charge $Z_A$ and $Z_B$ with dielectric constant ($D$) is given [24] by:

$$\frac{\partial \ln k}{\partial(1/D)} = -\text{Constant} \,.\, Z_A \,.\, Z_B$$

If the rate of the reaction which causes X to tail is proportional to $[H^+][WO_4^{2-}]$, *i.e.*,

[23] Erdmen and Erlenmeyer, *Helv. Chim. Acta*, 1954, **37**, 2220.
[24] Glasstone, Laidler, and Eyring, "The Theory of Rate Processes," McGraw-Hill, N.Y., 1941, p. 430.

$Z_AZ_B = -2$, the rate in 1 : 1 water–ethanol will be about one-fifth of that in water. On the other hand, if the rate of decomposition of Y ($HW_6O_{21}^{5-}$) is proportional to [$OH^-$], *i.e.*, $Z_AZ_B = 5$, the rate of conversion into the normal tungstate ion would be expected to be about 100-fold faster than in water. Thus there would be a considerably greater conversion of paratungstate A into normal tungstate on paper than *vice versa*. Whilst the dielectric constant cannot be regarded as the only factor which can cause changes in reaction rate when the species are absorbed on paper, this prediction is in fact observed; but the interconversion rate is still less, by at least a factor of ten, than could be accounted for by the changes in dielectric constant alone.

(c) *Effect of* pH.—The concentrations of the different species in solutions of different

FIG. 3. *Quantitative identification of components in a linear radioactivity profile.*

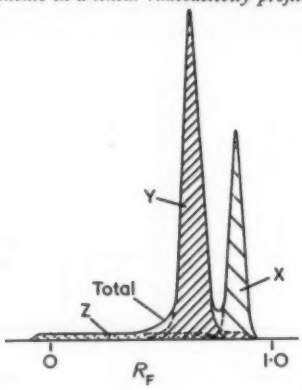
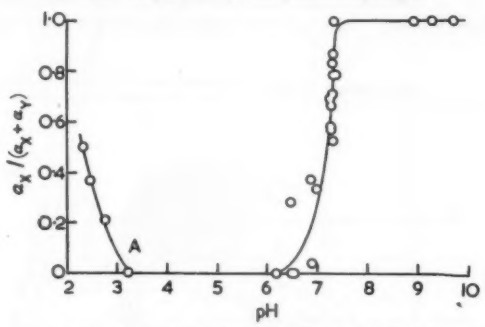



FIG. 4. *Dependence of composition upon* pH.




*$a_X$ and $a_Y$ are the percentages of tungsten as $WO_4^{2-}$ and $HW_6O_{21}^{5-}$, respectively.*

pH were determined by the chromatographic analysis of samples removed during the potentiometric titration at 25° of 2·00N-hydrochloric acid against 0·0192M-sodium tungstate containing a 10% (molar) excess of sodium hydroxide. Since the pH of acidified tungstate solutions increases slowly with time, all samples were kept overnight before measurement of the pH and chromatographic separation. The increased formation of component Z (paratungstate B) makes it undesirable to leave the solutions longer since this leads to increased tailing in the chromatogram and thus uncertainty in the quantitative analysis. There was found to be about 30% of component Z over the entire range of pH studied.

The results have been expressed in Fig. 4 by plotting $a_X/(a_X + a_Y)$ where $a_X$ and $a_Y$ are respectively the atom percentages of tungsten as $WO_4^{2-}$ and $HW_6O_{21}^{5-}$. Since it is not possible to distinguish between X and V by chromatography, any contribution from the latter will be included in $a_X$. In the pH range above 6—8, formation of V is not significant, but below pH 3·5 the presence of V undoubtedly accounts for the rising edge (A) of Fig. 4. Nevertheless it is apparent that the equilibrium $WO_4^{2-} \rightleftharpoons HW_6O_{21}^{5-}$ is markedly dependent on pH.

(d) *Time for Equilibration.*—The rate of formation of Z at 25° has been measured as a function of pH; a freshly acidified mixture of ~0·1M-sodium tungstate with an ~10% (molar) excess of sodium hydroxide was used for the kinetic studies. The results, shown in Fig. 5, are compared with similar results obtained by Souchay [10] by polarographic methods. Souchay approached equilibrium from both directions, first as in this work, and secondly by dissolution of solid sodium paratungstate [25] ($5Na_2O,12WO_3,28H_2O$) in water: he concluded that equilibrium is established in about one month. The chromatographic results, however, show that Z (paratungstate B) is still increasing in concentration even after

[25] Vallance, *J.*, 1931, 1421; Saddington and Cahn, *J.*, 1950, 3526; also ref. 1*i*.

this time. This suggests that Z also contains another polytungstate which is not intermediate in the formation of paratungstate A and paratungstate B, but is formed slowly from them. This would account for Dawihl's observation [26] that the solubility of ammonium paratungstate increases with time, equilibrium not having been established even after 14 months.

(e) *Properties of the Paratungstate A Anion.*—(i) pH *range of stability.* From Fig. 4 it can be seen that the paratungstate A ion, $HW_6O_{21}^{5-}$, is present in aqueous solution between pH 3·2 and 6·2. Above pH 7·5, the $WO_4^{2-}$ ion predominates, whilst below pH 3·2 there are appreciable quantities of the pseudo-metatungstate ion $H_3W_6O_{21}^{3-}$ (V) present. These results are analogous to the change [7] in self-diffusion coefficient between pH 5 and pH 9. It should be noted, however, that Souchay's polarographic results [10] are not in agreement with all the quantitative aspects of Fig. 4. In 0·1M-solutions (with respect to $WO_3$) he found 10% of the tungsten was present as the pseudo-metatungstate at pH 6·0 and about 90% at pH 5·0. This does not agree with our observation that in freshly prepared solutions this species is absent for pH >3·2.

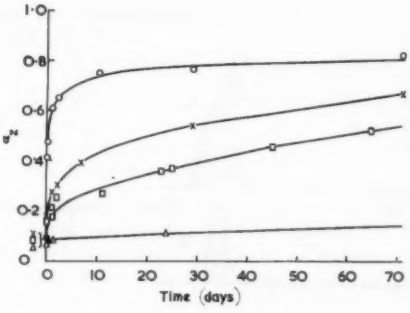



FIG. 5. *Formation of form* Z *in aged, acidified, sodium tungstate solutions.* A, pH 1·1. B, pH 5·0. C, pH 6·0. D, pH 6·8.

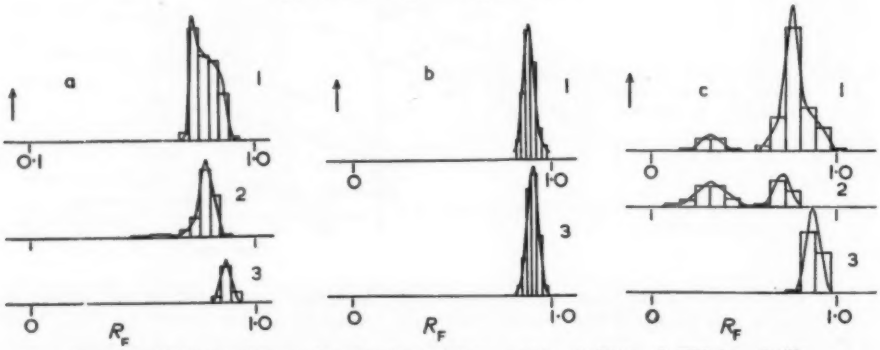
(ii) *Dimensions of the paratungstate A anion.* Anderson and Saddington [7b] found the self-diffusion coefficient of the normal tungstate anion to be $7{\cdot}7 \times 10^{-6}$ cm.$^2$ sec.$^{-1}$ and of the paratungstate A anion to be $3{\cdot}5 \times 10^{-6}$ cm.$^2$ sec.$^{-1}$. Recent electrochemical work [27] has shown that these results should be interpreted as due, not to a variation in mass, but to a variation in size. If the ions are considered as spherical balls, the radius calculated from Stokes's law or from Ottar's formula [27] is for $WO_4^{2-}$ 5·3 Å, and for $HW_6O_{21}^{5-}$ 12 Å. If the normal tungstate ion were tetrahedral, its unhydrated ionic radius would be about 2·9 Å. The average unhydrated radius of the condensed species is difficult to assess because of its unknown structure. If a 6-tungsten ring structure is assumed it would have a mean radius of about 5·0 Å, and the maximum radius across the ring would be about 5·8 Å. In comparing these figures, it should be noted that (*a*) both experimental figures are probably too high, since the self-diffusion coefficients determined by the capillary method are undoubtedly too low, perhaps even by a factor of 2; this would cause a greater relative error in the estimated radius for the condensed tungstate, for which mixing by diffusion would be less, and it would also explain the shallower slope of the plot of self-diffusion coefficient against pH [7c] than we obtained for $a_X/(a_X + a_Y)$ (Fig. 4), (*b*) both ions would be hydrated in solution, and the condensed ion may well be of sufficiently high charge to influence water molecules in more than the first hydration shell.

(iii) *Charge on the paratungstate A anion.* The relative mobility of the paratungstate A ion and the normal tungstate ion on paper was determined by electrophoresis. Although it is often asserted that this method gives an indication of the relative charges of the

[26] Dawihl, *Z. anorg. Chem.*, 1940, **244**, 1; *Chem. Abs.*, 1941, **35**, 2773.
[27] Ottar, *Acta Chem. Scand.*, 1955, **9**, 344; Stokes, *Rev. Pure Appl. Chem.* (*Australia*), 1955, **5**, 60; Baker and Pope, *J. Amer. Chem. Soc.*, 1960, **82**, 4176.

migrating species, we find it inapplicable to the present case. The results show that the tungsten does not move as far along the paper under acid as under alkaline conditions. Since the paratungstate A anion migrates more slowly than $WO_4^{2-}$, it is not possible to say whether it has a larger or a smaller charge. Undoubtedly the large difference in size contributes to this observation. A more direct method of estimating the charge of the paratungstate A anion was to analyse the chromatograms for sodium, tungstate, and chloride ion. The results are shown in Fig. 6. At high pH, the close proximity of the chloride to the $WO_4^{2-}$ (Fig. 6a) caused the sodium to overlap both, making it impossible to decide how much sodium was associated with each component. The distribution of the sodium ions is unexpected, but the experimental error is sufficiently small for it to be real. The front of the chloride spot contains twice as much chloride as sodium, *i.e.*, it apparently contains free hydrochloric acid. The centre of the tungstate peak is sodium-deficient compared with $Na_2WO_4$. A similar effect is shown with a chromatogram of pure sodium chloride (Fig. 6b), where the chloride leads the sodium by about 1 mm. These chromatographic results are not, however, unique. Thilo [20] found a single peak

FIG. 6. *Analysis of chromatograms.* (a) *Sodium tungstate at* pH 8·08. (b) *Sodium chloride.* (c) *Sodium tungstate at* pH 7·55.




*Arrows denote increasing number of moles (arbitrary scale).* 1, $Na^+$. 2, $WO_4^{2-}$. 3, $Cl^-$.

due to sodium in his separation of polyphosphates, even though about ten anionic components were separated.

It is thus impossible to estimate the charge on the polyanion from Figs. 6a and 6b. But at lower pH (Fig. 6c), where both the normal ion and the paratungstate ion are present, there are two sodium peaks. The first is between, but overlapping, both the chloride and the $WO_4^{2-}$ peaks. The second is associated exclusively with the paratungstate A anion, appears to have uniform composition, and is well separated from the other components. We can with some confidence, therefore, use these results for determining the sodium : tungsten ratio as $(0{\cdot}6 \pm 0{\cdot}1) : 1$, *i.e.*, if form Y is the hexatungstate, its composition would be approximately $Na_{(3{\cdot}5 \pm 0{\cdot}5)}H_{(3{\cdot}5 \pm 0{\cdot}5)}W_6O_{21}$. Whilst the polytungstate ion can apparently be associated with three or four sodium ions on paper, the lack of a quantitative theory of paper chromatography makes it difficult to extrapolate this result into aqueous solutions. Nevertheless, it is clear that the polyanion must be highly charged ($Z > 3$) in water, and this is confirmed by theoretical electrochemical considerations. Under the conditions of Fig. 6c, the paratungstate anion would form a loose association with cations of the Bjerrum type; [28] and, if reasonable values for the ionic radius and the activity coefficients [29] are used at the concentrations employed for Fig. 6c, each polyanion would be associated with $3{\cdot}8 \pm 0{\cdot}3$ sodium ions.

[28] Robinson and Stokes, "Electrolyte Solutions," Butterworths, London, 1959, 2nd edn., p. 392.
[29] Duncan and Kepert, *J.*, in the press.

*Conclusions.*—It has been shown that the paper-chromatographic method of separation of the components of a polytungstate solution can be used for the quantitative analysis of the solution, provides auxiliary information about the structure and properties of the components, and can be done with milligrams or less of material. An important and general point is that this separation and analysis can be achieved even though the components are in rapid equilibrium in aqueous solution. Part II of this series [29] will deal with use of the method for quantitative investigation of the equilibrium between the normal tungstate anion and the paratungstate A anion, for which the free energy, enthalpy, and entropy changes have been evaluated, and certain possible modes of reaction eliminated.

One of us (D. L. K.) acknowledges the tenure of a Commonwealth Postgraduate Scholarship when part of this work was done. The other (J. F. D.) acknowledges financial support for several years for radiochemical-inorganic work from the Australian Atomic Energy Commission.

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MELBOURNE, AUSTRALIA. [*Received, December 21st,* 1960.]

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## 1051. *Controlled-potential Electrolysis. Part VII.*[1] *Polarographic Behaviour and Controlled-potential Electrolysis of* 1,1-*Dinitroethane and Dinitromethane.*

By MASAICHIRO MASUI and HIROTERU SAYO.

1,1-Dinitroethane and dinitromethane showed three polarographic waves in very strong acid, two in acid, one in neutral, and two in alkaline solutions. By controlled-potential electrolysis with a mercury pool cathode 1,1-dinitroethane and dinitromethane were reduced mainly to acethydroxamic and formhydroxamic acid oxime by 6-electron reduction, and in alkaline solutions further to acetamidoxime and formamidoxime, respectively, by 8-electron reduction. These results enable the polarograms of both compounds to be interpreted.

THE polarography of *gem*-dinitroparaffins seems to have been discussed only by Radin and DeVries [2] and by Stock,[3] and the mechanism of the reduction and the interpretation of the polarograms have not yet become clear. In the preceding Part [1] we reported work on a dinitro-compound which has no hydrogen atom at the carbon carrying the nitro-groups, so that these cannot assume an *aci*-nitro-form. In the present paper, we have studied dinitro-compounds which can assume an *aci*-nitro-form.

### RESULTS

*The Polarography of* 1,1-*Dinitroethane.*—The results of the polarographic study of 1,1-dinitroethane are shown in Figs. 1 and 2 and Table 1. The sum of the heights of the first and the second waves in acid and alkaline solutions is nearly equal to those of the single waves in neutral solutions, except that at pH 4 the second wave is very poorly defined. The relation between the limiting currents and the mercury column heights (Table 2) shows that currents are not diffusion-controlled. The wave form in neutral solution is the best and the limiting current is proportional to the concentration between $4 \times 10^{-5}$ and $4 \times 10^{-4}$ mole $l.^{-1}$. The half-wave potentials of the first wave, in contrast to those of 2,2-dinitropropane, varied markedly with pH of the solution near its $pK_a$, but not much on either side of it. The diffusion-current constant estimated from the wave height in neutral solution is 10·75, being 3·5 times larger than that of the two-electron reduction of 2,2-dinitropropane in alkaline solution. The electron

[1] Part VI, *J.*, 1961, 4773.
[2] Radin and DeVries, *Analyt. Chem.*, 1952, **24**, 971.
[3] Stock, *J.*, 1957, 4532.

number of the reduction of 1,1-dinitroethane is, therefore, expected to be much larger than two.

*The Polarography of Dinitromethane.*—The results of the polarographic study of dinitromethane are shown in Figs. 3 and 4 and in Table 3. Its behaviour resembles closely that of 1,1-dinitroethane, but the half-wave potentials are slightly more positive and the single wave

TABLE 1.

Half-wave potentials and diffusion-current constants of 1,1-dinitroethane.

| pH | | 2·0 * | 4·0 | 6·0 | 8·0 | 10·0 | 12·0 |
|---|---|---|---|---|---|---|---|
| First wave: | $E_{\frac{1}{2}}$(v *vs.* S.C.E.) ... | −0·331 | −0·378 | −0·579 | −0·679 | −0·730 | −0·765 |
| | $i_d/Cm^{\frac{2}{3}}t^{\frac{1}{6}}$ ..... | 5·29 | 5·74 | 10·30 | 10·75 | 5·38 | 3·32 |
| Second wave: | $E_{\frac{1}{2}}$(v *vs.* S.C.E.)... | −0·806 | −0·828 | | | −1·390 | −1·490 |
| | $i_d/Cm^{\frac{2}{3}}t^{\frac{1}{6}}$ ..... | 3·85 | 1·43 | | | 5·38 | 6·90 |

* A poorly defined third wave exists at −1·151 v.

TABLE 2.

Effect of mercury column height on $i_d$ of 1,1-dinitroethane, $i_d h^{-\frac{1}{2}}$.

| | $h$ (cm.) | 40 | 50 | 60 | 70 | | $h$ (cm.) | 40 | 50 | 60 | 70 |
|---|---|---|---|---|---|---|---|---|---|---|---|
| pH 2; | first wave | 0·385 | 0·382 | 0·378 | 0·372 | pH 12; | first wave | 0·261 | 0·247 | 0·232 | 0·221 |
| | second wave | 0·258 | 0·263 | 0·270 | 0·277 | | second wave | 0·490 | 0·509 | 0·516 | 0·526 |
| pH 6; | first wave | 0·751 | 0·757 | 0·762 | 0·765 | | | | | | |

TABLE 3.

Half-wave potentials and diffusion-current constants of dinitromethane.

| pH | | 2·0 | 4·0 | 6·0 | 8·0 | 10·0 | 12·0 |
|---|---|---|---|---|---|---|---|
| First wave: | $E_{\frac{1}{2}}$(v *vs.* S.C.E.) ... | −0·280 | −0·443 | −0·632 | −0·708 | −0·719 | −0·720 |
| | $i_d/Cm^{\frac{2}{3}}t^{\frac{1}{6}}$ ..... | 6·54 | 12·46 | 12·53 | 5·61 | 2·64 | 2·53 |
| Second wave: | $E_{\frac{1}{2}}$(v *vs.* S.C.E.)... | −0·665 | | | −1·283 | −1·339 | −1·405 |
| | $i_d/Cm^{\frac{2}{3}}t^{\frac{1}{6}}$ ..... | 5·54 | | | 6·54 | 9·14 | 9·35 |

* A poorly defined third wave exists at −1·075 v.

TABLE 4.

Effect of mercury-column height on $i_d$ of dinitromethane, $i_d h^{-\frac{1}{2}}$.

| | $h$ (cm.) | 40 | 50 | 60 | 70 | | $h$ (cm.) | 40 | 50 | 60 | 70 |
|---|---|---|---|---|---|---|---|---|---|---|---|
| pH 2; | first wave | 0·481 | 0·481 | 0·478 | 0·466 | pH 10; | first wave | 0·204 | 0·195 | 0·191 | 0·191 |
| | second wave | 0·386 | 0·382 | 0·381 | 0·379 | | second wave | 0·651 | 0·647 | 0·630 | 0·619 |
| pH 6; | first wave | 0·949 | 0·945 | 0·941 | 0·931 | | | | | | |

develops at pH 4—6 instead of pH 6—8. The dependency of the limiting currents on the mercury-column height (Table 4) indicates that the currents are not diffusion-controlled. The sum of the heights of the two waves in acid or alkaline solution is almost the same as that of the single wave at pH 4 and 6.

*Controlled-potential Electrolysis of* 1,1-*Dinitroethane.*—(a) *Electrolysis in alkaline solution.* When 1,1-dinitroethane was electrolysed in 0·1N-aqueous sodium hydroxide with the potential of the mercury cathode at −1·7 v *vs.* S.C.E. (at the plateau of the second wave) the current–time curve exhibited a long tailing curve and a fairly long time was required for complete electrolysis. The amount of electricity required for the reduction corresponded to 8-electron reduction. If reduction began with C–N bond fission as did that of 2,2-dinitropropane, the resulting *aci*-form of the nitroethane and nitrite ion could not be reduced further; nor could these products react with each other in such conditions; so the electricity required should correspond to 2-electron reduction. We conclude that reduction proceeds without C–N bond fission. From the electrolysed solution only 0·1 molar equiv. of nitrite ion was found [4] and nitrate or ammonium ions could not be detected. On addition of concentrated sulphuric acid and distillation, acetic acid,[5] but no aldehyde,[6] was detected. The acetic acid is thought not to be derived

[4] Snell and Snell, " Colorimetric Methods of Analysis," D. van Nostrand Company, Inc., New York, 3rd edn., Vol. II, 1954, p. 804.
[5] Feigl, " Spot Tests," Elsevier Publ. Co., Amsterdam, 4th edn., Vol. II, p. 247.
[6] Ref. 5, p. 146; and by the 2,4-dinitrophenylhydrazine test.

from the nitroparaffin itself because no polarographic wave developed when the electrolysed solution was acidified as above. The solution was then made alkaline again and distilled; the distillate then contained ammonia. From these results the reduction product was expected to be an acetic acid derivative which could be hydrolysed by acid to acetic acid and ammonia. The ultraviolet absorption spectrum of the solution at first showed an absorption band of 1,1-dinitroethane at 382 mμ whose intensity decreased during the electrolysis while a new

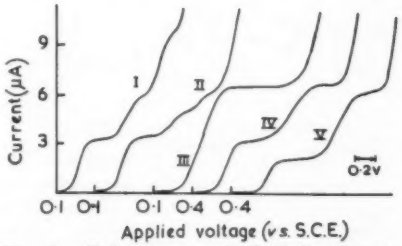


FIG. 1. Polarograms of 1,1-dinitroethane. pH: (I) 2·0; (II) 4·0; (III) 6·0; (IV) 10·0; (V) 12·0.

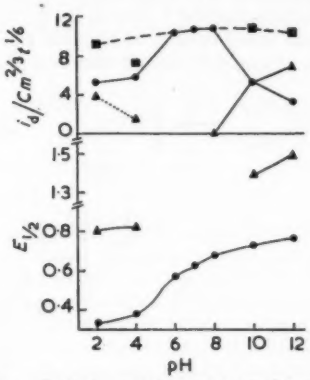


FIG. 2. Relation of $E_{\frac{1}{2}}$ and $i_d/Cm^{\frac{2}{3}}t^{\frac{1}{6}}$ to pH for 1,1-dinitroethane.

● First, ▲ second wave; ■ sum of the two.

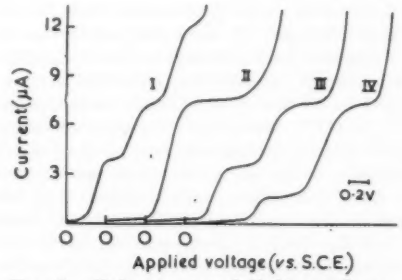


FIG. 3. Polarograms of dinitromethane. pH: (I) 2·0; (II) 6·0; (III) 8·0; (IV) 12·0.

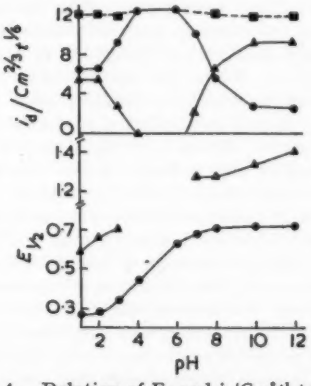


FIG. 4. Relation of $E_{\frac{1}{2}}$ and $i_d/Cm^{\frac{2}{3}}t^{\frac{1}{6}}$ to pH for dinitromethane.

● First, ▲ second wave; ■ sum of the two.

peak at 336 mμ appeared and increased in intensity; but this also later decreased and had disappeared at the end of the electrolysis.

Some of the more probable intermediates were prepared and examined. Ethanenitrolic acid (II) which appeared to be the product at the first stage of the reduction showed in 0·1N-NaOH a peak at 323 mμ (ε 8000) and polarographic waves of $E_{\frac{1}{2}} = -0{\cdot}816$ and $-1{\cdot}355$ v (*vs.* S.C.E.), the latter wave being ill-defined. Electrolysis of ethanenitrolic acid under our conditions required electricity corresponding to a 6-electron reduction and there was the same behaviour of the 336 mμ band as for dinitroethane. As a further reduction product acethydroxamic acid oxime (III) was expected; it was synthesised as hydrochloride; it did not

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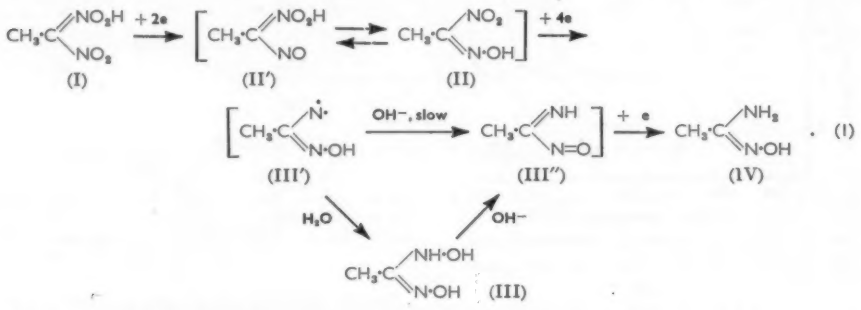
show reduction waves or ultraviolet absorption in acid solution but in alkaline solution gave an anodic wave of $E_{\frac{1}{2}} = -0{\cdot}278$ v and two cathodic waves of $E_{\frac{1}{2}} = -0{\cdot}468$ and $-1{\cdot}268$ v (*vs.* S.C.E.) and an absorption band at 336 mμ (ε 17,000). The electrolytic reduction required two electrons per molecule and the absorption peak decreased in intensity during the reduction. There was no indication of the production of ethylazaurolic acid ($\lambda_{max.}$ 348 mμ) which was expected to be formed from the oxime (III) in alkaline solution. From the electrolysed solution, acetamidoxime (IV) was obtained, which was identical with an authentic sample prepared by Nordmann's method [7] (mixed m. p. and infrared spectrum). Acetamidoxime did not give a reduction wave in acid or alkaline solution, nor was there any ultraviolet absorption around 336 mμ. From these results the most probable reduction scheme may be expressed by scheme (1).



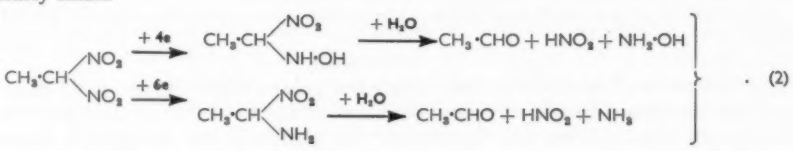

First, 1,1-dinitroethane undergoes two-electron reduction, regardless of whether it is in *H-aci*-form or *aci*-ion form, to ethanenitrolic acid (II) or (II′), which is reduced spontaneously by four-electron reduction to (III′) at the electrode, since the reduction potential of the second wave of (II) is more positive than that of (I). (III′) changes into (III″) which undergoes two-electron reduction to acetamidoxime (IV).

Compound (III) is thought to be converted into (III″) and both exist in alkaline solution, because: (1) though the hydrochloride synthesised is stable in water, it liberates a little nitrite ion when the solution is acidified after once being made alkaline; (2) the strong absorption at 336 mμ should be attributed to the nitroso-group conjugated with a double bond, as the form (III) cannot develop a strong absorption at that wavelength; and (3) the polarogram shows both anodic and cathodic waves, the former thought to be due to a hydroxylamino-group. The form produced by the electrolysis is assumed to be (III′), but it is rather hard to reduce because it contains merely a hydroxylamine and an oxime component but no conjugated system. It seems necessary that (III′) should change into an easily reducible one such as (III″) before it undergoes further reduction; and since this step is rather slower than the preceding ones, the behaviour of the absorption band at 336 mμ during the electrolysis can be explained. Controlled-potential electrolysis at $-1{\cdot}0$ v (*vs.* S.C.E.) (at the plateau of the first wave), though it took a very long time to proceed nearly to completion, decreased the height of the second polarographic wave as well as of the first one, and the behaviour of the absorption band at 336 mμ was identical with that described above except that it did not disappear completely. This implies that in the solution 1,1-dinitroethane, and also ethanenitrolic acid, are in equilibrium between two forms, one of which is easily and the other difficultly reducible, and as the concentration of 1,1-dinitroethane decreases it is supplied from the difficultly reducible form. The reduction scheme is, therefore, not different from the preceding one up to the (III″) stage, but here the lower applied potential causes a slower rate of reduction, and the potential is lower than that of the second wave for (III) in alkaline solution, so that the reduction is not brought quite to completion; the absorption band at 336 mμ, therefore, did not disappear.

(b) *Electrolysis in acid solution.* 1,1-Dinitroethane was electrolysed in the solution of pH 2 at $-0{\cdot}90$ v (*vs.* S.C.E.) (on the plateau of the second wave) and required the electricity corresponding to about a 5·6- instead of an 8-electron reduction. Nitrous acid was detected in the electrolysed solution. When the solution was made alkaline (pH 12·5), it developed the absorption peak at 336 mμ and also showed the polarogram of the acethydroxamic acid oxime (III),

[7] Nordmann, *Ber.*, 1884, **17**, 2747.

though the amount evaluated therefrom was only about 0·6 molar equivalent. As this oxime is not reducible in acid solution, the deficiency in the resulting solution could be caused by the following factors: (1) Ethane-nitrolic or -nitrosolic acid [which is thought to be an intermediate between the nitrolic acid and (III′)] is unstable in acid solution and part of it is decomposed before reduction at the electrode. (2) Part of the dinitroethane is reduced in a different way. Both factors are proved to be operative by the following facts. The electrolysed solution when heated with a small amount of concentrated sulphuric acid and distilled gave 0·1 equivalent of acetaldehyde. Since no acetaldehyde is produced by the processes of eqn. (1), another scheme such as (2) which contains no compound with a C=N bond should be considered, but its contribution is clearly small.



(2)

Electrolysis at −0·55 v (*vs.* S.C.E.) (on the plateau of the first wave) required a long time for completion and the number of electrons consumed per molecule was 5·3. The polarogram of the solution showed a gradually decreasing height of the second wave as well as of the first wave. The ultraviolet spectrum and the polarogram of the resulting solution in alkaline state were the same as those of the acethydroxamic acid oxime (III) described above. These results resemble closely those of electrolysis at −1·0 v in 0·1N-sodium hydroxide. The amount of the oxime (III) thus found was estimated to be 0·5 equiv. and was less than that obtained at a higher applied voltage. This is explained by the greater probability of decomposition of the intermediates owing to the slower reduction and thus the longer time for interaction with the acid solution. It is therefore concluded that the reductions of 1,1-dinitroethane appearing as the first and the second wave in the polarography, both in the alkaline and acid solution, do not require consecutive reduction steps as is the usual case, but are caused by the existence of the equilibrium between two forms and the rate of its attainment.

The poorly defined third wave in the solution of pH 2 is due to the reduction of nitrite ion produced by decomposition of the components, because on electrolysis at −1·15 v no nitrite ion was detected though the ultraviolet spectrum and the polarogram showed the presence of 0·55 equivalent of the oxime (III) in the solution as above.

(c) *Electrolysis in neutral solution.* As the polarogram in neutral solution was a simple single wave, the reduction mechanism was also thought to be simple, but the controlled-potential electrolysis did not give a simple result. The electron number for the reduction was 5·5, so the reduction does not proceed further than the oxime (III). Examination of the electrolysed solution as above showed that the amount of this oxime was only about 0·1 molar equivalent and that of nitrite about 0·23 equivalent. In the distillate from the acidified solution a very small amount of acetaldehyde and a large amount of acetic acid (0·76 equivalent) were found. The amount of acetic acid formed suggests that reduction takes the same course as in alkaline and acid solution. The deficiency in the oxime (III) is interpreted by its decomposition and/or by non-electrolytic reactions of (III), (III′), or (III″) which occur in the neutral condition producing substances having no absorption band near 336 mμ and giving no polarographic wave. The fact that during the electrolysis the intensity of the 336 mμ band passed a maximum supports this interpretation, but the nature of the substance produced is not known.

*Controlled-potential Electrolysis of Dinitromethane.*—(a) *Electrolysis in alkaline solution.* Electrolysis in 0·1N-sodium hydroxide at −1·7 v (*vs.* S.C.E.) consumed electricity corresponding to an ~8-electron reduction, 0·1 molar equivalent of nitrite being formed. The absorption band of dinitromethane at 365 mμ decreased in intensity during the electrolysis; a band at 334 mμ appeared and increased but disappeared by the end of the electrolysis. These observations are closely similar to those for 1,1-dinitroethane and a precisely similar reduction scheme is proposed.

Formhydroxamic acid oxime HO·NH·CH:N·OH, when synthesised, showed an absorption band at 334 mμ in alkaline solution as expected and formamidoxime $NH_2$·CH:N·OH, which was also prepared, did not. From the electrolysed solution crystalline formamidoxime was isolated.

(b) *Electrolysis in acid solution.* Electrolysis at −0·76 v in a solution of pH 2 required the

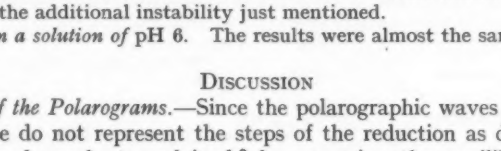
electricity corresponding to a 6·0-electron reduction. Nitrous acid was detected in the final solution. The absorption band at 334 mμ did not develop when the electrolysed solution was made alkaline to pH 12·5. As formhydroxamic acid oxime is very unstable in acid, it would be expected to decompose rapidly in this reaction. Detection of formaldehyde [8] in the electrolysed solution suggests that a small part of the dinitromethane was reduced according to a scheme analogous to scheme (2).

The electrolyses at the potentials on the plateau of the first and the third wave gave 5·5 and 11, respectively, as the electron numbers; there was no absorption band at 334 mμ in either case and no nitrous acid was formed in the latter. These results are explained as for dinitroethane, with the additional instability just mentioned.

(c) *Electrolysis in a solution of* pH 6. The results were almost the same as for 1,1-dinitroethane.

## Discussion

*Interpretation of the Polarograms.*—Since the polarographic waves of 1,1-dinitroethane and dinitromethane do not represent the steps of the reduction as described above, the polarograms obtained are best explained [9] by assuming the equilibrium expressed by scheme (3) and a fairly rapid attainment of equilibrium.

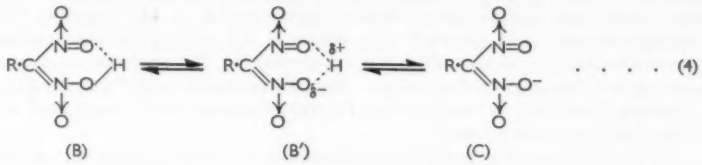



In very alkaline solution the compound takes a form (C) which shows a strong absorption band at 382 mμ (R = Me), and in very acid solutions under the polarographic conditions almost all of the compound exists as (A) since this band is diminished in intensity and instead the weak absorption of the nitro-form appears at 273 mμ. The negative charge on the nitro-group of (C) causes the reduction potential to be more cathodic, as for carboxylic acids,[10] and the second wave in alkaline solution is assigned to form (C). Because the inductive effect of one nitro-group on the other in form (A), as in general, does not make the reduction potential as positive as the resonance effect in form (B) does, form (B) should be regarded as the more easily reducible form. The second wave in acid solutions, therefore, is regarded as the reduction wave of (A), and the first wave which develops an S-shaped curve extending over all pH regions in its $E_{\frac{1}{2}}$–pH plots (Figs. 2 and 4) is attributed to the reduction of form (B). The above results and the fact that interconversion between the forms is fast, explain the behaviour of wave height in respect of pH (Figs. 2 and 4) and the formation, on electrolysis, of much acetic acid at all pH's and a little aldehyde in acid and none in alkaline solution. Reviewing the examples [11] we have found S-shaped $E_{\frac{1}{2}}$–pH curves to occur when the reduction contains a kinetic current process derived from the equilibrium between an easily (*e.g.*, undissociated) and a difficultly reducible (*e.g.*, dissociated) form, the slope of the curve being steepest in the pH region around $pH = pK_a$. In the present study the $E_{\frac{1}{2}}$–pH relation of the first wave has the same characters. The $pK_a$ values of 1,1-dinitroethane and dinitromethane, determined potentiometrically, are 5·27 and 3·74, respectively. The steepest slopes in Figs. 2 and 4 are at about the same pH regions and their values are about the same.

From these observations, the behaviour of the first wave and the split-wave phenomenon observed in alkaline region can be attributed to the equilibrium between the *H-aci*-nitro-form and the ionized *aci*-nitro-form. As form (C) represents the second wave in

[8] Ref. 5, p. 240.
[9] Cf. Turnbull and Maron, *J. Amer. Chem. Soc.*, 1943, **65**, 212.
[10] Kolthoff and Lingane, "Polarography," Interscience Publ. Inc., New York, 1952, pp. 269, 729.
[11] (*a*) Elving, Rosenthal, and Kramer, *J. Amer. Chem. Soc.*, 1951, **73**, 1717; Elving, *ibid.*, 1957, **79**, 1546; (*b*) Elving and Rosenthal, *Analyt. Chem.*, 1954, **26**, 1454; (*c*) Gergely and Iredale, *J.*, 1951, 3502.

alkaline region, the continuous increase of $E_{\frac{1}{2}}$ of the first wave in the pH region around pH = p$K_a$ requires an intermediate such as (B′) between (B) and (C) [scheme (4)].




. . . . . (4)

The first wave in acid solutions is attributed to (B) and that in alkaline solutions to (B′), and the charge expressed as $\delta^-$ in (B′) increasing with pH makes (B′) more difficultly reducible than (B). In other words, form (C) recombines with a proton to produce (B) or (B′). The magnitude of $\delta^-$ depends on the pH of the solution. As attainment of equilibrium is fairly fast, the amount of (B) consumed is supplied from (A) or/and (C), and this contributes to the height of the first wave, which is much greater than expected from its p$K_a$ value or from its absorption band; it decreases the height of the second wave, and in a certain pH region only one wave is observed. The rates of recombination of the *aci*-nitro-anion with a proton for dinitroethane and dinitromethane are calculated to be about $8 \times 10^7$ and $3 \times 10^5$ l. mole$^{-1}$ sec.$^{-1}$, respectively, by the method used for carboxylic acids.[11b,12]

The total wave heights in acid and alkaline solution and the height of a single wave near neutral region are almost constant except that the height at pH 4 for dinitroethane is highly affected by its ill-defined form. If the diffusion constant $D$ of 1,1-dinitroethane, calculated by the relation [13] $D\sqrt{M} = D'\sqrt{M'}$, where $M$ is the molecular weight and $D'$ and $M'$ refer to 2,2-dinitropropane, is correct, $n$ values estimated for dinitroethane by means of the Ilkovic equation for the total height are 6·7 and 7·0 at pH 6 and 12, respectively. If the 2-electron reduction from (III) to (IV) observed on controlled-potential electrolysis in alkaline solution occurs fully at the dropping-mercury electrode, the $n$ value should be substantially larger than in acid or neutral solution. The almost constant wave height with pH shown in Fig. 2 and 4 implies that the 2-electron reduction does not take place at the dropping-mercury electrode in the basic region to the extent of being easily recognized; and if it could occur the lower diffusion constant of highly charged species [11b] would compensate for the increments due to the reduction. In any case, the $n$ value for the total wave height should be closer to 6, even though a value of *ca.* 7 is derived from the Ilkovic equation.

## Experimental

*Materials.*—1,1-Dinitroethane potassium salt, prepared by reaction [14] between bromonitroethane and methanolic potassium hydroxide, had m. p. 151° (decomp.) (from water). Dinitromethane potassium salt,[15] prepared from dibromodinitromethane, arsenious acid, and potassium hydroxide, had m. p. 205° (decomp.) (from water). Ethanenitrolic acid,[16] prepared from nitroethane and nitrous acid, had m. p. 86° (decomp.) (from ether–light petroleum). Acethydroxamic acid oxime hydrochloride,[17] obtained from acethydroxamoyl chloride and hydroxylamine, had m. p. 154° (decomp.) (from ethanol–ether). Potassium ethanenitrosolate,[18] prepared by adding methanolic potassium hydroxide to acethydroxamic acid oxime hydrochloride, had m. p. 207° (decomp.) (from dilute aqueous ethanol). Acetamidoxime hydrochloride,[7]

[12] Delahay, " New Instrumental Methods in Electrochemistry," Interscience Publ. Inc., New York, 1958.
[13] Riehl and Wirths, *Z. phys. Chem.*, 1944, *B*, **194**, 97.
[14] Wieland and Sakellarios, *Ber.*, 1919, **52**, 904.
[15] Macbeth and Orr, *J.*, 1932, 539.
[16] Meyer and Constam, *Annalen*, 1882, **214**, 329.
[17] Wieland, *Annalen*, 1907, **353**, 86.
[18] Wieland, *Annalen*, 1907, **353**, 93.

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prepared from acetonitrile and hydroxylamine hydrochloride, had m. p. 140° (from ethanol–ether). Ethylazaurolic acid,[18] prepared by reduction of ethanenitrolic acid with sodium amalgam, had m. p. 142° (decomp.) (from ethanol). Formamidoxime [19] obtained from potassium cyanide and hydroxylamine hydrochloride, had m. p. 115° (decomp.) (from ethyl acetate). Formhydroxamic acid oxime [20] was prepared by adding hydroxylamine hydrochloride to formamidoxime; as it was not obtained crystalline, the reaction solution separated from the ammonium chloride formed was used. Methanenitrosolic acid,[20] prepared by adding methanolic potassium hydroxide to the solution of formhydroxamic acid oxime, had m. p. 194° (decomp.) (from dilute aqueous ethanol).

All the compounds (except formhydroxamic acid oxime) gave correct analysis.

*Apparatus.*—The apparatus for polarography and controlled-potential electrolysis, and the buffer solutions for the polarographic studies were the same as those used in the previous studies.[1] Dropping-mercury electrode having $m^{\frac{2}{3}}t^{\frac{1}{4}} = 1{\cdot}395$ was used. Polarographic measurements were carried out at 25° ± 0·1°.

A Toadempa Model HM-5 pH meter with glass S.C.E. was used for p$K_a$ determinations which were carried out on solutions more dilute than $4 \times 10^{-3}$ mole l.$^{-1}$.

A Beckman DU type spectrophotometer and Hitachi automatic recording spectrophotometer EPS-2 were used for ultraviolet spectroscopy, but only the former for the quantitative determinations.

Infrared spectra were obtained by using a Hitachi EPI-2 double-beam prism spectrophotometer.

*Controlled-potential Electrolysis of* 1,1-*Dinitroethane.*—(*a*) 1,1-Dinitroethane potassium salt (63·3 mg.) was electrolysed as usual in 0·1N-sodium hydroxide (200 ml.) at −1·7 v. The current was at first 600 mA and decreased to 5 mA in about 1·5 hr. During the electrolysis the ultraviolet spectrum of the solution was measured from time to time by pipetting 0·5 ml. of the solution and diluting it 20-fold. The electricity required was estimated from the current–time curve, the amount (304 coulombs) corresponding to 7·89 electrons per molecule. In this 0·5 ml. 0·12 equivalent of nitrous acid was determined.[4] Similarly electrolysed solutions of four runs were combined and acidified to pH 4 by dilute hydrochloric acid, then evaporated under reduced pressure at ~40°, and the residue was extracted with dry ethanol. The extract was evaporated again and the residue again extracted with dry ethanol. The precipitates produced on adding dry ether to the solution recrystallised from ethanol–ether. The m. p., 140° (decomp.), of the resulting product was not depressed on admixture with acetamidoxime prepared by Nordmann's method.[7] The samples gave identical infrared spectra ($\nu_{max.}$ 3322s, 3215s, 1684s, 1629m, 1059m cm.$^{-1}$).

For the electrolysis at −1·0 v (*vs.* S.C.E.) in 0·1N-sodium hydroxide the compound (63·5 mg.) was dissolved in 200 ml. of solution. The current was at first 140 mA and decreased to 5 mA in about 4 hr. The electricity required was 250 coulombs, corresponding to 6·45 electrons per molecule.

(*b*) The compound (63·3 mg.) was electrolysed at −0·9 v (*vs.* S.C.E.) in 0·1M-phosphoric acid–sodium hydroxide buffer solution (200 ml.) of pH 2 containing 0·1M-potassium chloride. The current, 250 mA at the beginning of the run, decreased to 2 mA after 1 hr. Electricity required was 216 coulombs, corresponding to 5·6 electrons per molecule. The electrolysed solution exhibited a reduction wave of $E_{\frac{1}{2}} = -0{\cdot}45$ v (*vs.* S.C.E.) when made alkaline with 20% aqueous sodium hydroxide to about pH 12·5. The alkaline solution was diluted 20-fold and examined for the absorption band at 336 mμ.

Electrolysis at −0·55 v was performed on 63·2 mg. of the compound, which consumed 202 coulombs for 1·5 hr., corresponding to 5·24 electrons per molecule.

(*c*) The compound (63·3 mg.) was electrolysed for 50 min. at −1·0 v in 0·1M-phosphate buffer solution (200 ml.) of pH 6 containing 0·1M-potassium chloride. The electricity consumed was 211 coulombs, corresponding to 5·47 electrons per molecule. A portion of the electrolysed solution was made alkaline as above to about pH 12·5 and its ultraviolet spectrum and polarogram were investigated.

*Determination of Acetic Acid.*—A solution was electrolysed as above, sulphamic acid (200 mg.) and a sufficiency of concentrated sulphuric acid were added, and the whole was distilled. The distillate was titrated with 0·1N-sodium hydroxide (phenolphthalein), then with 0·1N-silver

[19] Nef, *Annalen*, 1894, **280**, 320.
[20] Wieland and Hess, *Ber.*, 1909, **42**, 4178.

nitrate potentiometrically after addition of 2 drops of concentrated nitric acid. The difference of the two titration gave the amount of the acetic acid.

*Controlled-potential Electrolysis of Dinitromethane.*—(*a*) The compound (72·1 mg.) was electrolysed in 0·1N-sodium hydroxide (200 ml.) at −1·7 v (*vs.* S.C.E.). The current was 560 mA at the beginning and 2 mA after 80 min. From time to time the absorption spectrum of portions of the solution was measured after 50-fold dilution. The electrolysed solutions from five runs were combined, brought to pH about 7·2 with 10% hydrochloric acid, and evaporated at ~35°. The residue was extracted with anhydrous ethanol and the extract evaporated to dryness, and this residue extracted with ethyl acetate. Evaporation and recrystallization from ethyl acetate gave formamidoxime, m. p. 114° (decomp.) Found: C, 19·7; H, 6·6; N, 46·6. Calc. for $CH_4N_2O$: C, 20·0; H, 6·7; N, 46·65%), $\nu_{max.}$ 3401s, 3205s, 1675s, 1613m, 1316m, 958m, and 885m cm.$^{-1}$ (coincident with maxima of formamidoxime prepared by Nef's method).

For the electrolysis at −1·0 v of 31·6 mg., 138 coulombs, corresponding to 6·53 electrons per molecule, were required for 3 hr.

(*b*) The compound (28·8 mg.) was electrolysed in 200 ml. of the buffer solution of pH 2 used in (*b*) above, at −0·76 v (*vs.* S.C.E.). The current was 130 mA at the beginning and less than 2 mA after 1 hr. The electricity consumed was 116 coulomb, corresponding to 6·01 electrons per molecule. 20% sodium hydroxide solution was also used to bring the solution to pH 12·5.

For the electrolysis at −0·55 v 29·8 mg. of dinitromethane were used. 117 coulombs, corresponding to 5·86 electrons per molecule, were required for 1·5 hr.

(*c*) The compound (28·8 mg.) was electrolysed at pH 6; 116 coulombs, corresponding to 6·01 electrons per molecule, were consumed. Other operations were as described above.

We thank Professor K. Takiura for his interest.

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## 1052. *Polysaccharides of the Characeae. Part IV.*[1] *A Non-esterified Pectic Acid from* Nitella translucens.

By D. M. W. ANDERSON and N. J. KING.

The pectic complex extractable from the fresh-water green alga *Nitella translucens* contains a non-esterified pectic acid. This is best purified by precipitation as the copper complex, followed by incubation with α-amylase to remove contaminating glucans. The pectic acid had $[\alpha]_D$ +245° and contained 74% of uronic anhydride; hydrolysis gave galacturonic acid, with galactose, arabinose, xylose, and rhamnose in the ratio 4 : 6 : 3 : 1. Partial hydrolysis indicated that a high proportion of the arabinose and xylose residues were labile, the galactose being resistant to hydrolysis. Passage through diethylaminoethylcellulose gave one main fraction only. Methylation studies established the presence of chains of 1,4′-linked-α-D-galacturonic acid. This pectic acid is of interest in studies of the ion-exchange capacity of the algal cell-wall.

RECENT studies[1] revealed that the fresh-water green algæ *Nitella translucens* and *Chara australis* have clear similarities to higher terrestrial plants on the basis of their carbohydrate content. This is of interest since the botanical relationship of the *Charaphytae* to (*a*) *Chlorophytae* and (*b*) higher terrestrial plants is debated.[1]

The cell-walls of *Chara* and *Nitella* contain significant quantities of pectic materials;[1] these appear to perform ion-exchange functions similar to those of pectins in the roots of

[1] Parts II and III, Anderson and King, *Biochim. Biophys. Acta,* 1961, **52**, 441, 449.

higher terrestrial plants.[1] Pectin has so far not been isolated from marine sources.[2] The precise function of pectic materials in plant cells has long been in question.[2] When it was found that the pectic acid in these Characeae was non-esterified, it became important to establish the extent of its differences from the known plant pectic acids. Algal polysaccharides have previously provided many novel structural features:[3,4] indeed, *N. translucens* contains also an interesting labile starch-type glucan.[5]

The origin and collection of the alga, analyses of the dried cells (MeO $\gtrsim$ 0·1%), and the extraction procedures have been described.[1] Although the material extracted by water at 90° (fraction N5, ref. 1) contained 10·6% of galacturonic acid and had no methoxyl content, it was shown (Table 1, ref. 1) that this fraction accounted for only 1% of the total uronic anhydride content of the cells. Negligible amounts of pectic substances were therefore extracted in the hot-water and other preliminary treatments. In general, the lower the methoxyl content, the more difficult is the hot-water extraction of pectic substances from plant tissues.[6]

Extraction of the algal residues with hot aqueous ammonium oxalate–oxalic acid solution[7] gave ammonium pectate. Paper chromatography of a hydrolysate showed that galacturonic acid, galactose, glucose, arabinose, xylose, and rhamnose were present (Found: $[\alpha]_D$ +205°; uronic anhydride, 51%; Ac, $SO_4$, and OMe, 0). Despite attempted purification by precipitation with organic solvents, cetylpyridinium bromide, ammonium sulphate, as the calcium salt, and as the copper complex, no fractionation was achieved and none of the neutral sugars originally present was eliminated. Regeneration from the copper complex gave the best product, having $[\alpha]_D$ +240°, uronic anhydride 72% (both as free pectic acid). Subsequent incubation with salivary α-amylase removed the glucose-containing contaminant; the incomplete extraction of starch by cold and hot water[8] and the contamination of pectin by starch are well known.[9,10] The glucose-free pectic acid, which contained 74% of uronic anhydride, together with galactose, arabinose, xylose, and rhamnose in the ratio 4 : 6 : 3 : 1, was used in the experiments reported in this paper. Decarboxylation studies made later indicated[11] that this material had probably undergone about 8% of decarboxylation during its extraction (these studies assumed that all the carbon dioxide evolved came from 6-carboxyl groups).

Fractionation on a column of diethylaminoethylcellulose[12] gave one major component (see Table) which accounted for 74% of the material recovered from the column and for which the optical rotation, uronic anhydride, and proportions of neutral sugars were almost identical with those of the unfractionated material. Seventeen other fractions, none of which accounted for more than 2·5% of the material recovered, were also investigated. The significance of these must await further investigation with larger quantities of material; however, hydrolysis of some of the fractions eluted before the main peak gave two sugars of high chromatographic mobility (cf. refs. 13 and 14), and one of the fractions eluted after the main peak gave only galactose on hydrolysis, indicating that minor quantities of a galactan were present in the pectic complex (cf. ref. 2).

Hydrolysis at pH 5·0 with fungal pectinase gave the crystalline sodium–calcium double salt[15] of galacturonic acid in good yield. Partial hydrolysis (0·1N-hydrochloric

[1] Hirst and Jones, *Adv. Carbohydrate Chem.*, 1946, **2**, 235.
[2] Smith, *Ann. Reports*, 1956, **53**, 259.
[3] Hirst, *Proc. Chem. Soc.*, 1958, 177.
[4] Anderson and King, *J.*, 1961, 2914.
[5] Kertesz, "The Pectic Substances," Interscience Publ. Inc., New York, 1951.
[6] Williams and Bevenue, *J. Off. Agric. Chemists*, 1956, **39**, 901.
[7] Anderson and Greenwood, *J. Sci. Food Agric.*, 1955, **6**, 587.
[8] Taufel and Feldman, *Chem. Tech. (Berlin)*, 1954, **6**, 525.
[9] Bock, Baum, Döring, and Wardsack, *Ernährungsforsch.*, 1960, **5**, 539.
[10] Anderson, Bews, Garbutt, and King, *J.*, 1961, 5230.
[11] Neukom, Deuel, Heri, and Kundig, *Helv. Chim. Acta*, 1960, **43**, 64.
[12] Aspinall and Cañas-Rodriguez, *J.*, 1958, 4020.
[13] Aspinall and Fanshawe, 1961, 4215.
[14] Isbell and Frush, *J. Res. Nat. Bur. Stand.*, 1944, **32**, 77.

Fractionation of pectic acid on diethylaminoethylcellulose.

| Fraction | Total vol. eluted (ml.) | Wt. of fraction (mg.) | Sugars identified | | | | | $R_{rhamnose}$ of unidentified sugars (solvent C) |
|---|---|---|---|---|---|---|---|---|
| | | | Gal. Acid | Gal | Ara | X | Rha | |
| 1 | 40 | 2 | ++ | ++ | ++ | | + | |
| 2 | 220 | 7 | + | ++ | ++ | | + | |
| 3 | 420 | 7 | + | ++ | ++ | | + | |
| 4 | 670 | 4 | + | ++ | ++ | | + | |
| 5 | 690 | 3 | + | ++ | ++ | | | 1·21(+), 1·89(+) |
| 6 | 830 | 5 | + | ++ | ++ | | + | 1·24(+) |
| 7 | 960 | 6 | + | + | + | | | |
| 8 | 1130 | 7 | + | + | + | | + | 1·74(+) |
| 9 | 1150 | 3 | + | +++ | + | | | |
| Elution by sodium hydroxide begun. | | | | | | | | |
| 10 | 1350 | 10 | + | +++ | + | + | + | 1·22(+) |
| 11 | 1410 | 11 | + | ++++ | + | ++ | | oligos. ++ |
| 12 | 1560 | 3 | ++ | ++ | + | + | | oligos. ++ |
| 13 | 1610 | 9 | ++ | ++ | + | | | oligos. + |
| 14 | 1840 | 295 | 71% | + | + | | | oligos. +++ |
| 15 | 1930 | 9 | + | +++ | + | | | oligos. + |
| 16 | 2150 | 8 | + | +++ | | | | |
| 17 | 2250 | 9 | — | +++ | | | | |
| 18 | 2400 | 3 | — | +++ | + | | | |
| | | 401 | | | | | | |

acid, 2 hr., 100°) gave an insoluble, degraded polysaccharide having 83% of uronic anhydride; the sugars in the hydrolysate were galactose, arabinose, xylose, and rhamnose (3 : 10 : 6 : 1), with galacturonic acid also present. The pectic acid therefore contained labile arabinose and xylose. Further hydrolysis (2N-sulphuric acid, 6 hr., 100°) of the degraded polysaccharide gave galacturonic acid, and galactose, arabinose, xylose, and rhamnose (3 : 1 : 1 : 1), but hydrolysis was incomplete. Hydrolysis with 90% formic acid was also incomplete.

Periodate oxidation of the ammonium pectate required 1·05 moles of periodate per anhydrogalacturonic acid unit. The oxidised polysaccharide was reduced with sodium borohydride; chromatography of the hydrolysed product gave arabinose, xylose, and small amounts of galacturonic acid in addition to the expected threonic acid. The presence of arabinose and absence of galactose is in agreement with the structures proposed [2] for the araban and galactan components of pectic complexes. The unoxidised galacturonic acid may equally have arisen from incomplete periodate oxidation or from some galacturonic acid residues linked other than in the α-1,4′-manner commonly found in pectic acids.

Methylation of the pectic acid was difficult and was accompanied by extensive degradation: similar difficulties have been encountered previously.[2,16,17] Reasonable yields and methoxyl contents greater than 37—39% appear to be difficult to achieve with pectic materials (cf. refs. 13 and 16). After successive repeated treatments with thallium hydroxide–methyl iodide, dimethyl sulphate–sodium hydroxide, silver oxide–methyl iodide, a product having 37·4% of methoxyl (88% of the theoretical) was eventually obtained. After methanolysis, the product was reduced with lithium aluminium hydride, and the reduction product was hydrolysed. Chromatographic separation of the resultant mixture of sugars gave 7 fractions; from the two major fractions, crystals of the aniline derivative of 2,3-di-*O*-methyl-D-galactose were prepared.

Supplies of the authenticated alga are difficult to procure; only a limited amount of information could be obtained with the amount of material available, and it is hoped to obtain a larger supply in due course. It is apparent, however, that the pectic complex in *Nitella translucens* is similar in many respects to that from land plants, containing a pectic acid which has chains of 1,4′-linked α-D-galacturonic acid residues; these are

[16] Bishop, *Canad. J. Chem.*, 1955, **33**, 1521.
[17] Neukom and Deuel, *Chem. and Ind.*, 1958, 683.

XUM

not, however, present as methyl esters. This is clearly not the result of inadvertent demethylation or de-esterification during extraction, since the methoxyl content of the dried alga was >0·1%. The significance of this interesting pectic acid has been discussed [1] in relation to the lack of auxin-type hormonal activity in the *Nitellae* and to the possible ion-exchange function of these materials in the algal cell. The material may be of interest in investigations of the validity of current theories which relate the stability of pectins to their ester content.[18,19]

## Experimental

Paper partition chromatography was carried out on Whatman No. 1 paper with the following solvent systems (v/v): (A) butan-1-ol–benzene–pyridine–water (5 : 1 : 3 : 3, upper layer); (B) pyridine–ethyl acetate–acetic acid–water (5 : 3 : 1 : 3); (C) butan-1-ol–ethanol–water (4 : 1 : 5, upper layer); (D) butan-2-one, half saturated with water containing 1% of ammonia. Optical rotations were measured at 18° ± 2°. Uronic anhydride was found by Anderson's decarboxylation apparatus; [20] methoxyl by the vapour-phase infrared method; [21] nitrogen by Kjeldahl semimicro-determinations; ash by heating to constant weight at 550—600° (muffle).

*Isolation and Examination of the Water-soluble Polysaccharides.*—The origin and pre-treatment of the algal cells have been described, and the extraction scheme used has been detailed.[1] The yields and analytical results obtained for the cold- and hot-water extracts [1] show that insignificant amounts, if any, of the pectic content were extracted in these pre-treatments.

*Isolation and Examination of the Pectic Substances.*—The pectic substances were extracted from the cold- and hot-water residues by aqueous oxalate solution (0·25% with respect to both oxalic acid and ammonium oxalate [7]) at 80—90° for 1 hr. (three treatments) [yield, 31 g. of ammonium pectate from a batch of algal cells (dry wt. estimated at 320 g.)]. This crude product had $[\alpha]_D$ +205° (*c* 0·2 in $H_2O$), uronic anhydride 51%. After hydrolysis, chromatography showed that galacturonic acid was present, and also galactose, glucose, arabinose, xylose, and rhamnose (3 : 4·5 : 3 : 3 : 1).

*Purification and Attempted Fractionation of Ammonium Pectate.*—(1) The crude product (5 g.) was dissolved in water (400 ml.); ethanol, acidified with acetic acid (5 ml. per l.), was slowly added with stirring. Two fractions, which were not sharp, were collected: (A) at 40% ethanol, 3·7 g., $[\alpha]_D$ +220° (uronic anhydride, 60%); (B) at 60% ethanol, 0·8 g., $[\alpha]_D$ +220° (uronic anhydride, 65%). Reprecipitation failed to increase the uronic acid content significantly. Hydrolysis gave the same sugars as had been found in the crude product; the two fractions were therefore combined in view of their similarity.

(2) These combined fractions (3·8 g.) were dissolved in water, and 10% calcium chloride solution was added until precipitation of calcium pectate was complete. The precipitate was heated in water at 80° for 30 min. with a slight excess of ammonium oxalate; calcium oxalate was removed by filtration and the solution dialysed against distilled water. Pectic acid was precipitated by addition of acidified ethanol, isolated, then re-dissolved and re-precipitated a further three times. The product (3·4 g.; uronic anhydride, 64%) gave a cloudy solution, even after filtration through Celite on a No. 2 glass sinter. This was probably due to colloidal calcium oxalate; clarification was achieved by making the solution slightly alkaline, then adding sufficient ethylenediaminetetra-acetic acid to make the solution 0·05N in it. The ammonium pectate was precipitated after 30 min. by addition of ethanol, isolated, redissolved, and reprecipitated. This material had $[\alpha]_D$ +240° (*c* 0·3% in $H_2O$) (uronic anhydride, 69%); hydrolysis gave galacturonic acid, with galactose, glucose, arabinose, xylose, and rhamnose (4 : 1 : 5 : 4 : 1).

(3) Pectic acid (5 g.), a product of procedures 1 and 2 above, was dissolved in water and Fehling's solution added until precipitation of the copper complex was complete. Attempted decomposition of this complex, by adding it to 50% aqueous ethanol which was 4N with respect to acetic acid, removed only a little of the copper. The complex was therefore re-dispersed in water which was made just alkaline by sodium hydroxide; disodium ethylenediaminetetra-acetate was added and the mixture stirred at room temperature until the copper complex

[18] Whistler and BeMiller, *Adv. Carbohydrate Chem.*, 1958, **13**, 289.
[19] Albersheim, Neukom, and Deuel, *Arch. Biochem. Biophys.*, 1960, **90**, 46.
[20] Anderson, *Talanta*, 1959, **2**, 73.
[21] Anderson and Duncan, *Talanta*, 1961, **8**, 241.

dissolved. The sodium pectate was precipitated with ethanol, redissolved, and reprecipitated twice. The pectic acid (4·6 g.) finally isolated had $[\alpha]_D$ +240° (*c* 0·3% in $H_2O$) (uronic anhydride, 72; N, 0·16%).

(4) Ammonium sulphate (100 g.) was stirred into an aqueous solution (100 ml.) of a portion (2 g.) of the product from procedure (3) above. The solution was kept at 0° for 3 days. The precipitate was isolated, dissolved in water, and dialysed till free from salts. The pectic acid 1·6 g.), isolated in the usual way, had $[\alpha]_D$ +238° (*c* 0·2% in $H_2O$) (uronic anhydride, 68%).

(5) Cetylpyridinium bromide (1% aqueous solution) was added to a solution of ammonium pectate (a product of treatments 1 + 2) until precipitation was complete. This complex was very stable. Attempted regeneration of the pectic material by stirring it with 4N-acetic acid (400 ml.) for 1 hr. (three treatments) or 15% aqueous sodium chloride failed to dissolve the complex. Heating it at 60° with 0·5% aqueous ammonium oxalate was finally successful. The pectic acid finally obtained had $[\alpha]_D$ +205° (*c* 0·4% in $H_2O$) (uronic anhydride, 54%).

*Removal of Glucose.*—Each of the purified products described above gave a positive reaction with iodine solution and gave, on hydrolysis, galacturonic acid with galactose, glucose, arabinose, xylose, and rhamnose. Only the amounts of glucose present were variable. Digestion with salivary α-amylase, followed by dialysis, removed all the glucose-containing contaminant,[6,10] leaving the amounts of other sugars unchanged. The polysaccharide having the highest uronic anhydride content was obtained by treatment with α-amylase of the product from procedure (3) above. This pectic acid had $[\alpha]_D$ +245° (*c* 0·3% in $H_2O$) (uronic anhydride, 74%); hydrolysis and paper chromatography gave galactose, arabinose, xylose, and rhamnose (4 : 6 : 3 : 1), and galacturonic acid. The subsequent experiments were made on this material.

*Chromatography on Diethylaminoethylcellulose.*[12]—Pectic acid (420 mg.) was treated on a column (22 × 3 cm.) of diethylaminoethylcellulose, with gradient elution with phosphate buffer (pH 6, 0·5M, 750 ml. siphoning into 500 ml. of water, flow-rate 40 ml. per min.) followed by gradient elution with aqueous sodium hydroxide. The fractions (20 ml.) were screened for uronic anhydride content by the carbazole method.[22] The Table shows the sugars found in each fraction after dialysis, freeze-drying, hydrolysis, and chromatography: 401 mg. of material were recovered.

*Enzymic Hydrolysis.*—Crude fungal pectinase (50 mg.) was shaken with acetate buffer (0·1M, pH 5·0, 50 ml.); the filtrate was added to an aqueous solution of ammonium pectate (300 mg. in 100 ml.). After incubation at 37° for 2 days, the solution was concentrated to about 30 ml., then fractionated on a charcoal–Celite column [23] [2 × 30 cm.; Celite + ultrasorb ZF charcoal (1 : 1)]. Gradient elution was by aqueous ethanol (0·5—15%; total vol. 1·25 l. in 150 ml. fractions), then by aqueous pyridine (0·5—3%). The pyridine fractions were found to contain only galacturonic acid and were therefore combined and reduced in volume. After addition of sodium hydrogen carbonate (to pH 4·0) and calcium carbonate (1 g.), the mixture was heated at 80° for 10 min. Reduction in volume after filtration gave a thin syrup which crystallised (92 mg. of sodium calcium galacturonate hexahydrate [15]). From the free acid, the 2,5-dichlorophenylhydrazone, m. p. 179°, and mucic acid, m. p. 205°, were prepared; these derivatives had infrared spectra identical with those of authentic specimens.

*Periodate Oxidation.*—Ammonium pectate (190 mg.; $[\alpha]_D$ +240°, uronic anhydride, 69%) was oxidised at 2° in darkness with 0·025M-sodium metaperiodate (100 ml.). The reduction of periodate [24] (mol. per uronic anhydride unit) was: 0·32 (17 hr.); 0·47 (42 hr.); 0·77 (95 hr.); 0·94 (138 hr.); 1·05 (173 hr.); 1·06 (320 hr.). The periodate oxidation was repeated on a larger sample of pectate (490 mg.). Ethylene glycol (5 ml.) was added after 320 hr. and the oxidised polysaccharide was then treated with sodium borohydride (0·8 g.) overnight. The product was precipitated with ethanol, reprecipitated twice, then taken to dryness several times with small portions of methanol to remove borate {yield, 520 mg., $[\alpha]_D$ +36° (*c* 1·2% in $H_2O$)}. Dialysis against distilled water gave a dialysable fraction {160 mg., $[\alpha]_D$ +18° (*c* 1·6% in $H_2O$)} and a non-dialysable fraction {140 mg., $[\alpha]_D$ +10° (*c* 1·0% in $H_2O$)}. On hydrolysis by 0·5N-hydrochloric acid for 4 hr. at 100° each fraction gave the same products (paper chromatography; solvents A, B, and C)—galacturonic acid, arabinose, and xylose (galactose absent). With solvent C, the presence of threonic acid ($R_{rhamnose}$ 1·27) was indicated.

[22] Dische, "Methods of Biochemical Analysis," Interscience Publ. Inc., New York, 1951, Vol. II, p. 313.
[23] Whistler and Durso, *J. Amer. Chem. Soc.*, 1950, **72**, 677.
[24] Halsall, Hirst, and Jones, *J.*, 1947, 1399, 1427.

XUM

*Methylation of Ammonium Pectate.*—Complete methylation was difficult to achieve and several experiments were conducted with little success. Eight treatments with dimethyl sulphate and sodium hydroxide gave, in 26% yield, a product having 14·6% of methoxyl; three treatments with silver oxide and methyl iodide then gave, in 15% yield, a product having 32·3% of methoxyl. The best result (OMe, 37·4%; yield, 8%) was obtained by a procedure involving the use in turn of repeated treatments with thallium hydroxide–methyl iodide, dimethyl sulphate–sodium hydroxide, and silver oxide–methyl iodide.

*Fractionation of Methylated Methyl Pectate.*—Light petroleum (b. p. 40—60°) was added to a solution of the methylated polysaccharide (380 mg.) dissolved in chloroform (20 ml.), giving the following fractions:

| Ratio of chloroform to light petroleum | Fraction no. | Wt. of fraction (mg.) | $[\alpha]_D$ |
|---|---|---|---|
| 2 : 1 | I | 33 | +180° |
| 1 : 1 | II | 57 | — |
| 1 : 2 | III | 154 | +186 |
| Unprecipitated | IV | 110 | +123 |

*Methanolysis of Methylated Methyl Pectate; Reduction, Hydrolysis, and Separation of Methylated Sugars.*—Fraction III (154 mg.) was heated in a sealed tube with methanolic 6% hydrogen chloride (3 ml.) at 100° for 12 hr. After neutralisation (silver carbonate) and removal of solvent, the residue was extracted several times with chloroform. The resulting syrup was dissolved in dry tetrahydrofuran (15 ml.), and lithium aluminium hydride in tetrahydrofuran (0·2 g. in 10 ml.) was added dropwise to the boiling solution. After refluxing for 30 min., the solution was cooled and the excess of hydride destroyed by addition of ethyl acetate and water. The mixture was taken to dryness under reduced pressure, and the residue extracted with acetone and ethanol. The extracts were diluted with water, de-ionised, and reduced in volume to a syrup (107 mg.). This was hydrolysed with N-hydrochloric acid (5 ml.) at 100° for 4 hr. Neutralisation by silver carbonate, filtration, and evaporation gave a syrupy mixture of sugars (89 mg.). This was chromatographed on thick paper (50 × 15 cm., Whatman seed-test grade), upward development with solvent B being used to give seven fractions. After elution with hot 7 : 3 aqueous methanol, these fractions were reduced in volume and examined by paper chromatography and solvent B: two of the fractions contained three components and the remainder contained two components (cf. ref. 13) as shown below:

| Fraction | $R_{rhamnose}$, colour with aniline oxalate, and intensity | | | |
|---|---|---|---|---|
| a | 0·62 R–B +++ | 0·80 Y–B + | | |
| b | 0·63 R–B + | 0·81 R–B ++ | | |
| c | 0·63 R–B + | 0·80 R–B +++ | | |
| d | | 0·83 R–B +++ | 1·14 O–R +++ | |
| e | 0·60 R–B + | 0·86 R–B + | 1·17 O–R ++++ | |
| f | | 0·86 R–B + | 1·10 O–R + | 1·45 O–R +++ |
| g | | 0·82 R–B + | | 1·76 O–R +++ |

R–B, red-brown; Y–B, yellow-brown; O–R, orange-red.

The largest individual fractions were f and g. These were combined (total 35 mg.) and refluxed with aniline (0·5 ml.) in methanol (5 ml.) in darkness. From this, crystals, m. p. 151° (20 mg.), were obtained which were identical (infrared spectroscopy) with the aniline derivative of 2,3-di-*O*-methyl-D-galactose.

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# 1053. *The Oxidation of Organic Sulphides. Part X.*[1] *The Co-oxidation of Sulphides and Olefins.*

By D. Barnard, L. Bateman, M. E. Cain, T. Colclough, and J. I. Cunneen.

Certain organic mono- and di-sulphides retard the autoxidation of squalene. This retardation has been shown to be due, not to the sulphides themselves, but to the derived sulphoxides and thiolsulphinates, which are highly active when critical structural requirements are fulfilled.

Previous papers in this series have dealt with the oxidation of various types of organic sulphide by oxygen,[2] hydroperoxides,[3] and ozone.[1] We now describe the effect exerted by such sulphides on autoxidising hydrocarbons, that is, systems in which hydroperoxides could be formed *in situ* and which could exhibit distinctive features associated with co-oxidation phenomena.

Considerable interest attaches to the beneficial action exerted by organic sulphides on the stability of, for example, polyethylene [4] and lubricating oils [5] under oxidising conditions. This action has been ascribed to the ability of the sulphides,[6] or of the derived sulphonic acids,[7] to interact with and effectively to destroy the hydroperoxides which normally function as initiators of the free-radical oxidation chain process. We have found: (i) a highly specific dependence of inhibitory activity on sulphide structure which is inconsistent with the above postulate in its simplest form; and (ii) that it is not in fact the sulphides themselves which are active in this respect but certain oxygenated derivatives.

## Experimental

*Squalene.*—Basking-shark liver oil was twice distilled in a falling-film short-path still [8] and successively chromatographed, as a 2% solution in light petroleum (b. p. 30—40°), on alumina, activated charcoal, and alumina.

*Ethyl Linoleate.*—Material supplied by the Hormel Foundation and described as the pure *cis-cis*-isomer with less than 0·12% of conjugated diene was used as purchased.

*But-2-enylbenzene.*—A " research " grade supplied by Phillips Petroleum Co. was used without further purification.

*Sulphur Compounds.*—Except for the new compounds listed below, these were either commercial samples or were synthesised by standard methods. All were purified by fractional distillation or crystallisation.

1,3-*Diphenylallyl t-Butyl Sulphide.*—1,3-Diphenylallyl alcohol (0·1 mole) and 2-methylpropane-2-thiol (0·1 mole) were heated *in vacuo* at 75° for 16 hr. in a sealed tube. The product was dissolved in light petroleum (1 l.; b. p. 40°), dried ($MgSO_4$), and eluted from alumina (1·5 × 50 cm.). After removal of solvent the residual *sulphide* was distilled and had b. p. 166—168°/0·002 mm., $n_D^{20}$ 1·5991 (Found: C, 81·1; H, 7·90; S, 11·1. $C_{19}H_{22}S$ requires C, 81·4; H, 7·6; S, 11·0%), $\lambda_{max.}$ (in cyclohexane) 2570 Å (ε 21,400).

1,3-*Diphenylallyl Phenyl Sulphide.*—Prepared as above from 1,3-diphenylallyl alcohol and thiophenol, the *product* recrystallised from ethanol as colourless needles, m. p. 75·5—76° (Found: C, 83·0; H, 6·2; S, 10·5. $C_{21}H_{18}S$ requires C, 83·5; H, 6·0; S, 10·6%), $\lambda_{max.}$ (in cyclohexane) 2570 Å (ε 24,900).

*Preparation of Sulphoxides.*—A standard procedure [9] for the oxidation of the parent

[1] Part IX, Barnard, *J.*, 1957, 4547.
[2] (*a*) Bateman and Cunneen, *J.*, 1955, 1596; (*b*) Bateman and Shipley, *J.*, 1955, 1996; (*c*) Bateman, Cunneen, and Ford, *J.*, 1956, 3056; (*d*) Bateman, Cunneen, and Ford, *J.*, 1957, 1539.
[3] (*a*) Bateman and Hargrave, *Proc. Roy. Soc.*, 1954, *A*, **224**, 389; (*b*) Bateman and Hargrave, *ibid.*, p. 399; (*c*) Hargrave, *ibid.*, 1956, *A*, **235**, 55; (*d*) Barnard, *J.*, 1956, 489.
[4] Hawkins, Lanza, Loeffler, Matreyek, and Winslow, *J. Polymer Sci.*, 1958, **28**, 439.
[5] Denison, *Ind. Eng. Chem.*, 1944, **36**, 477; Kennerly and Patterson, *ibid.*, 1956, **48**, 1917.
[6] Denison and Condit, *Ind. Eng. Chem.*, 1945, **37**, 1102.
[7] Leonardi, Oberright, Orkin, and White, *Preprints Div. of Petroleum Chem., Amer. Chem. Soc.*, 1957, **2** (No. 1), 35.
[8] Farmer and Sutton, *J. Soc. Chem. Ind.*, 1946, **65**, 164.
[9] Barnard, Fabian, and Koch, *J.*, 1949, 2442.

sulphides with hydrogen peroxide in acetone was employed for the preparation of the following compounds.

| | B. p./mm. | $n_D^{20}$ | Purity from SO content [10] (%) |
|---|---|---|---|
| $Bu^t \cdot SO \cdot Bu^t$ | (M. p. 63·5—65°) | — | 98·0 |
| $Et \cdot CH{:}CH \cdot CH_2 \cdot SO \cdot Me$ | 43—44°/0·01 | 1·5038 | 97·8 |
| $CH_2{:}CH \cdot CHMe \cdot SO \cdot Bu^n$ | 55°/0·005 | 1·4935 | 97·5 |
| $Et \cdot CH{:}CH \cdot CHMe \cdot SO \cdot Me$ | 50°/0·01 | 1·4970 | 97·1 |
| Cyclohex-2-enyl t-butyl sulphoxide | * | — | 97·6 |

* Purified by counter-current distribution between light petroleum and water.

*t-Butyl 2-Methylpropane-2-thiolsulphinate.*—2-Methylpropane-2-sulphinic acid (22 g.), obtained by the reaction of t-butylmagnesium chloride with sulphur dioxide, was treated with thionyl chloride (25 ml.) to give *2-methylpropane-2-sulphinyl chloride* (19·8 g.), b. p. 62°/15 mm., $n_D^{18}$ 1·4840 (Found: C, 34·2; H, 6·4; Cl, 25·8; S, 23·1. $C_4H_9ClOS$ requires C, 34·1; H, 6·4; Cl, 25·2; S, 22·8%). Slow addition of a mixture of 2-methylpropane-2-thiol (1 mol.) and pyridine (1 mol.) to the sulphinyl chloride (1 mol.) in ether gave the *thiolsulphinate*, b. p. 55°/0·05 mm., $n_D^{21}$ 1·5060 (Found: C, 49·0; H, 9·3; S, 32·4. $C_8H_{18}OS_2$ requires C, 49·5; H, 9·4; S, 32·9%).

*Di-*[p-(*phenylsulphinylthio*)*phenyl*] *Ether.*—Benzenesulphinyl chloride (18·4 g.) in ether (200 ml.) was added slowly to a stirred suspension of bis-4-mercaptophenyl ether (12·8 g.), prepared by Marvel and Caesar's method,[11] in pyridine (9·05 g.) and ether (200 ml.) at −10°. After warming to room temperature the mixture was diluted with chloroform (150 ml.) to give a clear yellow solution. This was washed with 2N-sulphuric acid (150 ml.), dried ($CaCl_2$), and evaporated, to give a yellow solid (26·6 g.) which had a purity, as the expected *thiolsulphinate*, of 79·5%.[12] Recrystallisation from methanol–chloroform gave a product of purity 95%, as thiolsulphinate, m. p. 100—102° (decomp.) (Found: C, 59·7; H, 3·7; S, 26·5. $C_{24}H_{18}O_3S_4$ requires C, 59·7; H, 3·8; S, 26·6%).

1,3-Dimethylbut-2-enyl 1-ethyl-2-methylpropyl sulphide, 1,3-dimethylbut-2-enyl 1,1-dimethylbutyl sulphide, bis-(1,3-dimethylbut-2-enyl) sulphide and disulphide, and bis-(1,1-dimethylbutyl) disulphide were kindly presented by Dr. B. Saville.

*Oxidation Apparatus and Procedure.*—The absorption of oxygen was measured in a constant-pressure apparatus, essentially as described by Bateman and Cunneen.[2a] To ensure reproducibility of results it was necessary to pass both the olefins and liquid sulphur compounds through columns of alumina under a nitrogen atmosphere immediately before use. A standard concentration (0·25M) of sulphur compound in olefin and a standard temperature (75°) of oxidation were adopted, except in the case of certain of the more active materials when concentrations of 0·01M or less were used.

*Expression of Results.*—The usual plots of extent of oxidation *versus* either time or rate of oxidation were complex and no single parameter could be derived to express the effect of the additive. An arbitrary " retardation ratio " has been adopted, *viz.*, the ratio of the times taken for 1% (w/w) (or in certain specified cases 0·1%) of oxygen to be absorbed by the olefin plus additive, and by the pure olefin, respectively. The larger the ratio the better the performance of the additive as a retarder of oxidation.

## Results and Discussion

The effect of a wide variety of saturated and unsaturated mono- and di-sulphides and of other sulphur compounds on the autoxidation of squalene is expressed by the retardation ratios given in Tables 1—4. From these it will be seen that most monosulphides are without effect on the autoxidation under the conditions stated, but that a few exert a marked retardation. For highest activity the critical structural requirements are (*a*) that one substituent on the sulphur atom be a t-butyl (or other t-alkyl) group, and (*b*) that the second substituent be another t-butyl group (as in di-t-butyl sulphide) or an allyl group alkylated at the 1- and the 3-position (as in t-butyl 1,3,3-trimethylallyl and t-butyl cyclohexenyl sulphide). The reverse is apparent with the disulphides examined; that is, most show retarder activity but this is at its highest with simple alkyl disulphides and is

[10] Barnard and Hargrave, *Analyt. Chim. Acta*, 1951, **5**, 536.
[11] Marvel and Caesar, *J. Amer. Chem. Soc.*, 1951, **73**, 1097.
[12] Barnard and Cole, *Analyt. Chim. Acta*, 1959, **20**, 540.

TABLE 1.

Saturated monosulphides.

| Sulphide (0·25M) | Retardn. ratio | Sulphide (0·25M) | Retardn. ratio | Sulphide (0·25M) | Retardn. ratio |
|---|---|---|---|---|---|
| $Bu^n_2S$ | 1·7 * | 2-Ethyl-1,2,3,4-tetrahydro-5-isopropyl-2-methylthiophen | 3·7 * | $Bu^t_2S$ | 256 |
| $C_6H_{11}$·SMe | 3·4 * | $Bu^t$·SMe | 1·4 | $Bu^tS·CCl_3$ | 0·8 |
| Thiacyclohexane | 4·5 * | $Bu^t$·$SPr^i$ | 2·1 | $Bu^t$·SPh | 1·4 |
| | | | | $Ph_3C$·SPh | 0·7 |

* At 400 mm. oxygen pressure, otherwise at 760 mm.

TABLE 2.

Unsaturated monosulphides.

| Sulphide (0·25M) | Retardn. ratio | Sulphide (0·25M) | Retardn. ratio |
|---|---|---|---|
| $CH_2$:CH·$CH_2$·$SBu^n$ | 1·4 * | $CMe_2$:CH·CHMe·S·$CMe_2Pr^n$ | 357 |
| $CH_2$:CH·$CH_2$·$SBu^t$ | 1·5 | $CMe_2$:CH·$CMe_2$·$SBu^t$ | 110 |
| CHMe:CH·$CH_2$·SMe | 1·3 * | CHPh:CH·$CH_2$·$SBu^n$ | 6·3,* 3·5 |
| $CH_2$:CH·CHMe·$SBu^n$ | 4·1 * | CHPh:CH·CHPh·$SBu^t$ | 1·2 |
| CHMe:CH·CHMe·SMe | 3·8,* 3·1 | CHPh:CH·CHPh·SPh | 2·3 |
| CHMe:CH·CHMe·$SPr^i$ | 24·3 | Cyclohex-2-enyl methyl sulphide | 2·4 * |
| CHMe:CH·CHMe·$SBu^n$ | 40·5,* 15·3 | Cyclohex-2-enyl t-butyl sulphide | 480,* 150 |
| CHMe:CH·CHMe·$SBu^t$ | 310,* 93 | 1-Thiacyclohex-3-ene | 3·8 |
| CHMe:CH·CHMe·SPh | 270 * | 1-Thiacyclohex-2-ene | 6·9 * |
| $CMe_2$:CH·CHMe·S·CHEt·$CHMe_2$ | 110 | 2,3-Dihydro-2-isopropyl-5-methylthiophen | 3·6 * |
| $CMe_2$:CH·CHMe·S·CHMe·CH:$CMe_2$ | 4·4 | MeS·CH:CH·CHMe·S·Me | 1·1 |
| $CMe_2$:CH·CHMe·S·$CMe_2$·CH:CHMe | 5·0 | | |
| $CMe_2$:CH·CHMe·$SBu^t$ | 276 | | |

* At 400 mm. oxygen pressure, otherwise at 760 mm.

TABLE 3.

Di- and poly-sulphides.

| Sulphide (0·25M) | Retardn. ratio | Sulphide (0·25M) | Retardn. ratio | Sulphide (0·25M) | Retardn. ratio |
|---|---|---|---|---|---|
| MeS·SMe | 9 | Dicyclohex-2-enyl disulphide | 20 | $CH_2Ph$·S·S·$CH_2Ph$ | 8 |
| $Pr^iS$·$SPr^i$ | 66 | (Me·$[CH_2]_4$·$CH_2$·S·)$_2$ | 51 | Dibenzothiazol-2-yl disulphide | 5 |
| $Bu^nS$·$SBu^n$ | 121, 90 † | (Me·$[CH_2]_2$·$CMe_2$·S·)$_2$ | 1·7 | 1,2-Dithian | 7 |
| $Bu^tS$·$SBu^t$ | 1·6 | ($CMe_2$:CH·CHMe·S·)$_2$ | 9 | $Pr^iS$·S·S·$SPr^i$ | 79 |
| $C_6H_{11}$·S·S·$C_6H_{11}$ | 106 | PhS·SPh | 2 | | |

† At 760 mm. oxygen pressure, otherwise at 400 mm.

TABLE 4.

Miscellaneous sulphur compounds.

| Compound | Retardn. ratio | Compound | Retardn. ratio |
|---|---|---|---|
| Sulphur (0·25M) | 107 | 2,5-Diphenyl-1,4-dithiin 1-oxide (0·25M) | 17 |
| Ph·$SO_2$H (0·01M) | 1·8 | ($Me_2N$·$CS_2$)$_2$Zn (0·25M) | 128 |
| ,, (0·1M) | 1·4 | ($Me_2N$·$CS_2$)$_2$Zn (0·01M) | 28 |
| $Bu^t$·$SO_2$H (0·01M) | 1·0 * | [$Me_2N$·$CS_2$·]$_2$ (0·01M) | 17 |
| $Bu^t$·$SO_2$H (0·01M) | 0·6 * | Thiourea (0·01M) | 11 |
| $Et_2SO_3$ (0·01M) | 1·3 * | Phenothiazine (0·004M) | 415 * |
| Ph·SO·OMe (0·25M) | 1·0 | | |
| 2,5-Diphenyl-1,4-dithiin (0·25M) | 8 | | |

* At 760 mm. oxygen pressure, otherwise at 400 mm.

lost almost completely in the case of di-t-alkyl and diaryl disulphides. Among the miscellaneous sulphur compounds (Table 4), only sulphur itself, zinc dimethyldithiocarbamate (a powerful antioxidant [13]), and phenothiazine are strong retarders. Representatives of more conventional classes of antioxidant, phenyl-β-naphthylamine and β-naphthol, at concentrations of 0·01M gave comparable retardation ratios of about 100.

[13] Dunn and Scanlan, *Trans. Proc. Inst. Rubber Ind.*, 1958, **34**, 228.

XUM

*Basis of the Retarding Activity.*—If, as has been postulated,[6] the retarding activity merely reflects the reduction of olefin hydroperoxide by sulphide, then it would be predicted from detailed studies of this interaction [3a,b] that activity would be a maximum, not a minimum, with a di-n-alkyl monosulphide and would, in any case, be of a low order at the moderate temperatures employed.

What is truly responsible can be deduced from careful studies of the course of retarded reactions in the very early stages. Retardation was found to be imposed only after a

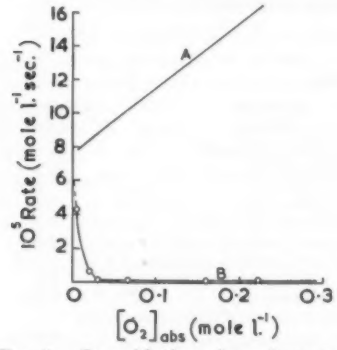
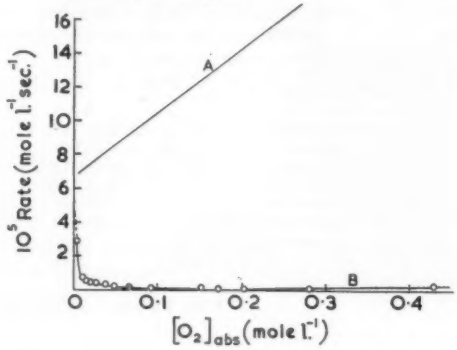



FIG. 1. Co-oxidation of squalene and cyclohexenyl t-butyl sulphide (0·25M) at 75° and 760 mm. oxygen pressure. (A) Squalene alone; (B) squalene plus sulphide.

FIG. 2. Co-oxidation of squalene and di-n-butyl disulphide (0·25M) at 75° and 400 mm. oxygen pressure. (A) Squalene alone; (B) squalene plus sulphide.



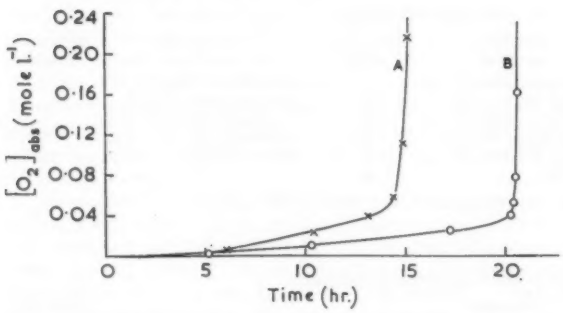




FIG. 3. Co-oxidation of squalene with (A) di-t-butyl sulphoxide (0·01M), and (B) n-butyl butanethiolsulphinate (0·005M) at 75°.

very small but quite definite absorption of oxygen (Figs. 1 and 2) implying that it is not the sulphides themselves but one or more oxidized derivatives which are the actual retarders and that these are of high potency. By direct test of the possible oxygenated derivatives, including sulphoxides, sulphones, thiolsulphinates, thiolsulphonates, disulphones, sulphinic and sulphonic acids, only those sulphoxides derived from the " active " monosulphides, and thiolsulphinates were found to be highly active. From the data in Table 5 and typical oxidation curves (Fig. 3) it will be seen that: (*a*) these derivatives are effective as retarders at much lower concentrations than are the parent sulphides; (*b*) retardation occurs from the earliest stages of reaction—there is no measurable initial absorption of oxygen necessary as with the sulphides; and (*c*) there is a much more abrupt ending of the induction period than with the sulphides (cf. Figs. 1 and 2). The length of the induction period is partly, at least, determined by the thermal instability of the retarder, which, especially for the sulphoxides,[14] runs parallel to activity. This instability is one

[14] Colclough and Cunneen, *Chem. and Ind.*, 1960, 626; and unpublished work.

cause of the non-linear dependence of retardation efficiency on concentration, and undoubtedly is involved in the more puzzling feature that in certain cases the retardation ratios pass through a maximum as the concentration is increased, behaviour which has been observed with other antioxidants.[15]

The identity of the true retarder was confirmed by isolating the sulphoxide from a large-scale oxidised mixture of squalene and cyclohexenyl t-butyl sulphide after counter-current distribution of the products between squalene and aqueous methanol. Only those fractions containing sulphoxide were immediately effective in producing an induction period when added to autoxidising squalene. In a similar experiment, in which squalene containing di-n-butyl disulphide (0·25M) was autoxidised until the maximum degree of retardation was achieved and the mixture then eluted in light petroleum from a column of silica gel, it was found that the recovered squalene, which still contained the major part of the disulphide, behaved as the original mixture, *i.e.*, retardation developed only after more oxygen was absorbed. The small amount of material eluted from silica gel with methanol caused immediate but short-lived (1 hr.) retardation of autoxidation when added to fresh squalene. n-Butyl butanethiolsulphinate was shown to be present in the eluate by paper-chromatography.[12] It was confirmed in separate experiments that thiol-sulphinates are normal products of the reaction of disulphides with hydroperoxides in the temperature range of present interest—their formation when peracids are the oxidants is well known.[16]

The conclusion is reached, therefore, that the co-oxidation of squalene with a mono- or di-sulphide commences with the normal formation of squalene hydroperoxide,[17] and that the latter, or intermediate peroxy-radicals, then react with the sulphide to yield the sulphoxide or thiolsulphinate. Oxygen uptake is then depressed to a value determined by (i) the efficiency of the sulphoxide or thiolsulphinate as inhibitor, (ii) the ease with which these compounds are formed under the oxidation conditions, and (iii) the readiness with which they undergo thermal decomposition under the same conditions.

*Structural Features Affecting the Retarding Activity of Sulphoxides and Thiolsulphinates.*—The data in Tables 1—3 and 5 show that all mono- and di-sulphides which are retarders yield sulphoxides and thiolsulphinates of high activity, but that the converse is not necessarily true. For example, diaryl and di-t-alkyl disulphides are inactive while the corresponding thiolsulphinates would be rated as active and highly active, respectively. The explanation for this lies in the relative resistance of these sulphides to oxidation by peroxides. More puzzling is the inactivity of isopropyl t-butyl sulphide even though its sulphoxide is one of the most active examined and its rate of oxidation by hydroperoxide is only slightly less than that of di-t-butyl sulphide. This apparent anomaly suggests a delicate interplay of the three factors mentioned above in determining sulphide activity.

In general, however, relations between structure and activity in the sulphoxides and thiolsulphinates parallel those in the parent sulphides, as discussed earlier. While all the thiolsulphinates examined show largely similar activities, there is a critical dependence on structure in the sulphoxides with the same combinations of t-alkyl and substituted allyl substituents required for high activity as in the monosulphides. This is to be expected as the latter are active only as a consequence of their oxidation to an active sulphoxide. The possible significance of the particular sulphoxide structures which confer high retarder activity will be discussed in a later paper.

*Effect of Reaction Conditions on Retarding Activity.*—Reduction of the temperature below 75° generally led to an increase in the retardation ratio. For sulphoxides and thiolsulphinates this can be attributed to their longer life at the lower temperatures. For sulphides the situation is more complex since the rate of formation of the active retarder will now influence the overall effect. For example, with di-n-butyl disulphide a lower

[15] Shelton, *Rubber Chem. Technol.*, 1957, **30**, 1251.
[16] Small, Bailey, and Cavallito, *J. Amer. Chem. Soc.*, 1947, **69**, 1711.
[17] Bolland and Hughes, *J.*, 1949, 492.

TABLE 5.

The inhibitory effects of the oxidation products of mono- and di-sulphides on the autoxidation of squalene at 75°.

| Additive | Concn. (M) | Retardn. ratio † | Additive | Concn. (M) | Retardn. ratio † |
|---|---|---|---|---|---|
| $CHMe{:}CH{\cdot}CH_2{\cdot}SO{\cdot}Me$ | 0·26 | 5 | $Bu^n{\cdot}SO{\cdot}SBu^n$ | 0·005 | 248, 32 * |
| $CH_2{:}CH{\cdot}CHMe{\cdot}SO{\cdot}Bu^n$ | 0·26 | 3 | $Et{\cdot}SO{\cdot}SEt$ | 0·004 | 145, 48 * |
| $CHMe{:}CH{\cdot}CHMe{\cdot}SO{\cdot}Me$ | 0·26 | 7 | ,, | 0·25 | 337, 83 * |
| $CMe_2{:}CH{\cdot}CHMe{\cdot}SO{\cdot}Me$ | 0·01 | 50, 11 * | $Bu^t{\cdot}SO{\cdot}SBu^t$ | 0·004 | 140, 140 * |
| $CMe_2{:}CH{\cdot}CHMe{\cdot}SO{\cdot}Pr^i$ | 0·01 | 310, 60 * | $Ph{\cdot}SO{\cdot}SPh$ | 0·005 | 40, 14 * |
| Cyclohex-2-enyl t-butyl sulphoxide | 0·26 | 69 | ,, | 0·01 | 68, 24 * |
| ,, ,, ,, | 0·005 | 112 | ,, | 0·05 | 372, 132 * |
| $Bu^n{\cdot}SO{\cdot}Bu^n$ | 0·01 | 1, 1 * | ,, | 0·15 | 487, 225 * |
| $Et{\cdot}SO{\cdot}Bu^t$ | 0·01 | 1, 1 * | ,, | 0·25 | 575, 240 * |
| $Pr^i{\cdot}SO{\cdot}Bu^t$ | 0·006 | 120, 90 * | ,, | 0·40 | 737, 156 * |
| $Bu^t{\cdot}SO{\cdot}Bu^t$ | 0·01 | 144, 24 * | Di-[*p*-(phenylsulphinylthio)-phenyl] ether | 0·005 | 33, 26 * |
| ,, | 0·03 | 95, 30 * | $Ph{\cdot}SO_2{\cdot}SPh$ | 0·25 | 1, 0·7 * |
| ,, | 0·06 | 59, 9 * | $Et{\cdot}SO_2{\cdot}SEt$ | 0·01 | 1, 1 * |
| $Bu^t{\cdot}SO{\cdot}CCl_3$ | 0·005 | 1, 1 * | $Ph{\cdot}SO_2{\cdot}SO{\cdot}Ph$ | 0·05 | 10, 20 * |
| $Bu^t{\cdot}SO_2{\cdot}Bu^t$ | 0·01 | 1, 1 * | $Ph{\cdot}SO_2{\cdot}SO_2{\cdot}Ph$ | 0·25 | 1, 1 * |
| Cyclohex-2-enyl t-butyl sulphone | 0·25 | 1, 1 * | | | |

* Retardation ratio calculated on times to 1% oxygen uptake.

† Retardation ratio calculated on times to 0·1% oxygen uptake. This often corresponds approximately to the end of the induction period.

temperature results in a poorer performance at low extents of oxidation but a superior performance at higher extents when thiolsulphinate has accumulated.

Retardation ratios found at 400 and 760 mm. oxygen pressure often differ appreciably (Tables 1 and 2), although the induction periods given by sulphoxides and thiolsulphinates are insensitive to this variation. The rate of autoxidation of squalene is nearly, but not quite independent of oxygen pressure in this range (at the pressures mentioned the times

TABLE 6.

Retardation ratios of sulphur compounds in various olefins at 75°.

| Additive (0·25M) | Retardation ratio | | |
|---|---|---|---|
| | Squalene | But-2-enylbenzene | Et linoleate |
| Di-n-butyl disulphide | 90 | 15 | 1·7 |
| Di-t-butyl sulphide | 256 | | 36 |
| Cyclohexenyl t-butyl sulphide | 150 | 16 | 32 |
| Phenyl benzenethiolsulphinate | 240 | 6 | 8 |

for the absorption of 1% w/w of oxygen are 42 and 36 minutes, respectively). It appears, therefore, that this slight difference in rate is sufficient to disturb what is clearly a critical balance in the relative build up of hydroperoxide and retarder. Some support for this view is that the time taken for maximum retardation to be produced by di-n-butyl disulphide is more affected by changes in oxygen pressure than is the actual degree of retardation.

*Effect of Olefin Structure.*—In certain olefins other than squalene the various sulphur compounds exert a much reduced activity under the present conditions (Table 6). This is in accord with the view that the olefin hydroperoxide is involved not only in the formation of retarder but also in the mechanism of retardation and that, therefore, its specific reactivity greatly influences the overall effect. A fuller discussion of this point will be presented later.

The authors acknowledge the contribution made by Dr. A. L. Morris to the early stages of this work.

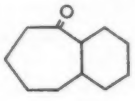
THE NATURAL RUBBER PRODUCERS' RESEARCH ASSOCIATION,
48–56 TEWIN ROAD, WELWYN GARDEN CITY, HERTS. [*Received, May 16th*, 1961.]

## 1054. *Synthetical and Stereochemical Studies in the Perhydrobenzocyclohepten-1-one System.*

By Dvora Kimchi and Shlomo Bien.

The preparation of 2,3,4,5,6,7,8,9-octahydrobenzocyclohepten-1-one (III)* is described, and the stereochemistry of its ketonic and alcoholic reduction products is determined.

The relative stabilities of several *cis*- and *trans*-fused α-ketonic bicyclo-systems, in which one of the rings is six-membered, are known. In the perhydroindan-1-one system the *cis*-isomer has proved to be the more stable,[1] but the reverse situation applies to α-decalone.[2] The next higher homologues, *cis*- and *trans*-perhydrobenzosuberone (I), were synthesised only a few years ago and the *trans*-ketone was the more stable.[3] The object of the present work was the synthesis and the stereochemical study of the hitherto unknown *cis*- and *trans*-perhydrobenzocyclohepten-1-ones (II).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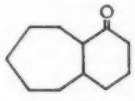
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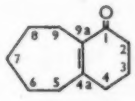
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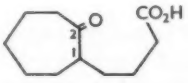
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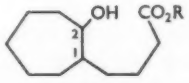
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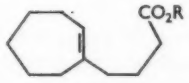
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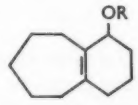

(VII)

A precursor (III) of both the *cis*- and the *trans*-isomer of compound (II) was synthesised from methyl 2-oxocycloheptanecarboxylate. This β-keto-ester was alkylated with methyl γ-bromobutyrate in the presence of sodium ethoxide in dry ethanol.[4] A second method, in which the carbanion was obtained by the use of metallic potassium in dry benzene,[5] gave large amounts of dimethyl suberate, formed by coupling of the halogeno-ester. Similar side reactions are common in the Reformatsky reaction.[6]

The alkylated keto-ester was hydrolysed and decarboxylated in one step by refluxing it with barium hydroxide solution, giving the keto-acid (IV), which was in turn purified through its semicarbazone. Reduction with sodium borohydride and esterification of the crude intermediate hydroxy-acid with diazomethane afforded the hydroxy-ester (V; R = Me), which was dehydrated by using phosphorus pentoxide in dry benzene or (best) phosphorus oxychloride and pyridine, or by boiling its toluene-*p*-sulphonate with collidine. Hydrolysis of the resulting ester (VI; R = Me), followed by cyclisation with acetic anhydride and zinc chloride in acetic acid, gave the desired unsaturated ketone (III) through the intermediate acid (VI; R = H).

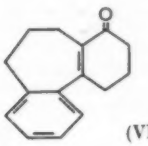
Analysis of the unsaturated ketone (III) showed low carbon and higher oxygen values, even after purification by chromatography and distillation, manganese dioxide oxidation

* The nomenclature used in this paper is that of I.U.P.A.C. rule A–21.4 [*Chem. Soc. Special Publ.* 14 (1960), p. 68] whereby benzocycloheptene denotes the 6,7-ring compound containing (formally) five double bonds.

[1] Linstead, *Ann. Reports*, 1935, **32**, 311.
[2] Hückel and Brinkmann, *Annalen*, 1925, **441**, 21.
[3] Ginsburg and Rosenfelder, *Tetrahedron*, 1957, **1**, 3; Gutsche and Peter, *J. Amer. Chem. Soc.*, 1955, **77**, 5971.
[4] Cf. Tinker, *J. Org. Chem.*, 1951, **16**, 1417.
[5] Büchi and Jeger, *Helv. Chim. Acta*, 1949, **33**, 538.
[6] " Organic Reactions," John Wiley and Sons, Inc., New York, 1947, Vol. I, p. 4.

of the corresponding allylic alcohol (VII; R = H) (obtained from ketone III by hydride ion reduction), or hydrolysis of the semicarbazone. On the other hand, its 2,4-dinitrophenylhydrazone, semicarbazone, and oxime, as well as its reduction product (VII; R = H), gave correct analyses. An analogous system [7] (VIII) and the lower homologue [8] (XI) showed the same analytical discrepancies.

It is known that under acidic cyclisation conditions, used in the last step of the synthesis, the double bond of an alkenoic acid is highly labile.[9] On the other hand, a double-bond shift might be expected in the cyclised product if a more stable compound is formed thereby. Consequently one must decide whether the resulting unsaturated ketone is (III) or (IX). In a very similar case, Campbell and Harris [10] assigned structure (X) to α-octalone on the basis of the ultraviolet absorption maximum observed at 243 mμ. In the light of Woodward's rules [11] (published later), no conclusive choice can be made between structures (X) and (XI), whose calculated absorption maxima are at 240 and 247 mμ respectively. More recently,[8] Quartey found $\lambda_{max.}$ 244 mμ for the same α-octalone and claimed structure (XI) for it. In the present work, the unsaturated ketone showed an absorption maximum at 249 mμ, which rules out structure (IX) and favours (III).



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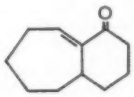

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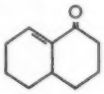
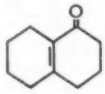


(X)



(XI)

The same structure (III) appears to be correct as the compound shows the following nuclear magnetic resonances: (*a*) a single sharp line at 438 c./sec. (7·31 p.p.m., τ = 2·69) which is the residual chloroform in the deuterochloroform used as solvent; (*b*) a complex multiplet at 141·7 c./sec. (2·36 p.p.m., τ = 7·64) representing the protons adjacent to the carbonyl group and those allylic to the double bond; (*c*) a complex multiplet at 97·3 c./sec. (1·62 p.p.m., τ = 8·38) representing the remaining methylene protons; (*d*) the single sharp line of the tetramethylsilane used as an internal standard. The compound shows no resonances, even at high gain, in the τ = 3·5—5·5 region in which one would expect to find any simple, cyclic conjugated or non-conjugated olefinic protons.

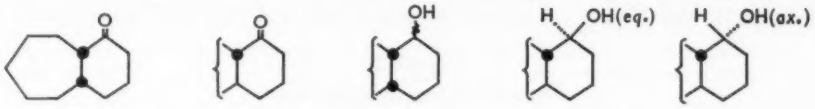
Catalytic reduction of compound (III) in a neutral medium led to a mixture of saturated ketones (subsequently referred to as mixture " A "), containing mainly one stereoisomer and altering its isomer ratio on alkaline equilibration. From molecular models, as well in analogy with perhydrobenzosuberone (I) and the well-investigated α-decalone system, we can expect the *trans*-ketone (XIII) to be the more stable stereoisomer.

Mixture " A " was directly reduced with lithium aluminium hydride to the corresponding alcohols, separable by chromatography on basic alumina. The *trans*-alcohols were eluted from the column in small amounts, followed by the main fraction of the *cis*-alcohol (XIV).* The latter was oxidised to the pure *cis*-ketone (XII) by chromic oxide in pyridine, a method proved to be stereospecific.[12] On the other hand, when mixture " A " was reduced after alkaline epimerisation, chromatography on basic alumina gave the *trans*-fused alcohols (XV) and (XVI) as the main products and only a minute amount

* All such formulæ include those of the mirror images.

[7] Crabb and Schofield, *J.*, 1958, 4276.
[8] Quartey, *J. Indian Chem. Soc.*, 1960, **37**, 731.
[9] Ansell and Brown, *J.*, 1958, 2955.
[10] Campbell and Harris, *J. Amer. Chem. Soc.*, 1941, **63**, 2721.
[11] Woodward, *J. Amer. Chem. Soc.*, 1941, **63**, 1123; 1942, **64**, 72, 76; Dorfman, *Chem. Rev.*, 1953, **53**, 59.
[12] Cope, Brown, and Hiok-Huang Lee, *J. Amer. Chem. Soc.*, 1958, **80**, 2855; Cope, Berchtold, Peterson, and Sharman, *ibid.*, 1960, **82**, 6371.

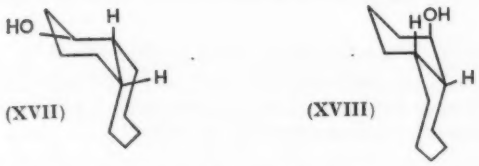
of *cis*-fused alcohol (XIV). Both *trans*-fused alcohols led to the same *trans*-fused ketone (XIII) on oxidation by chromic oxide in pyridine. The same *trans*-fused ketone resulted from the *cis*-fused isomer (XII) in high yield on epimerisation by sodium methoxide.




(XII) (XIII) (XIV) (XV) (XVI)

The rates of oxidation of the *trans*-alcohols, as well as those of saponification of their acetates, made it possible to assign to them the equatorial (XV) and the axial conformation (XVI), respectively. The axial epimer was eluted from the column before the equatorial, in accordance with the generality that equatorial alcohols are the more polar.[13] Their infrared spectra showed at 1046 and 1000 cm.$^{-1}$ the strong single bands characteristic of equatorial and axial C–O stretching frequencies, respectively.[14]

In the *cis*-series only one alcohol could be isolated; it showed the characteristic bands of both equatorial and axial alcohols at 1050 and 1010 cm.$^{-1}$, respectively. The compound may exist as an equilibrium mixture of the two conformations (XVII and XVIII) and possesses both equatorial and axial character, as is known in the case of *cis*-α-decalol.[15]




(XVII) (XVIII)

On hydrogenation of the unsaturated ketone (III) in acid or basic medium, the *cis*-isomer content of the resulting mixture was always lower than that of the hydrogenation mixture obtained in neutral medium. Reduction was apparently followed by epimerisation in both cases.

The unsaturated ketone (III) was then reduced with lithium and liquid ammonia, and a mixture containing preponderantly the *trans*-ketone (XIII) was obtained. When this reaction was repeated in the presence of absolute alcohol, the quantity of the *cis*-isomer in the resulting mixture (in this case the *cis*-alcohol) was greatly increased. This suggests that kinetically controlled protonation of the intermediate lithium enolate gave the unstable *cis*-isomer, as the main product. Several examples were given by Zimmerman [16] in which kinetically controlled ketonisation of enols leads to the formation of the thermodynamically less stable of two possible stereoisomers. Recently, a number of authors [16b,17,18] reported the formation of an unstable *cis*-epimer as the main product in the metal–ammonia reduction of αβ-unsaturated ketones and the formation of the *trans*-isomer was attributed to epimerisation occurring during the working up. This exploration was supported in the present work by showing that a new equilibrium mixture was obtained when a known mixture of saturated ketones was reduced with lithium and liquid ammonia.

[13] Barton and Cookson, *Quart. Rev.*, 1956, **10**, 44.
[14] Jones, Humphries, Herling, and Dobriner, *J. Amer. Chem. Soc.*, 1951, **73**, 3215; Dauben, Hoeringer, and Freeman, *ibid.*, 1952, **74**, 5206; Cole, Jones, and Dobriner, *ibid.*, 1952, **74**, 5571.
[15] Braude and Nachod, "Determination of Organic Structures by Physical Methods," Academic Press Inc., New York, 1955, p. 689.
[16] Zimmerman, (*a*) *J. Org. Chem.*, 1955, **20**, 549; (*b*) *J. Amer. Chem. Soc.*, 1956, **78**, 1168; (*c*) Zimmerman and Giallombardo, *ibid.*, p. 6259; (*d*) Zimmerman and Mais, *ibid.*, 1959, **81**, 3644.
[17] Birch, Smith, and Thornton, *J.*, 1957, 1339.
[18] Loewenthal, *J.*, 1958, 1367.

*Quantitative Infrared Analysis.*—The *cis* : *trans*-isomer ratios in the different ketone and alcohol mixtures were estimated by the method of Zimmerman *et al.*[16b,c,d] The *trans*-ketone had a strong peak at 1176 cm.$^{-1}$ and one of medium intensity at 913 cm.$^{-1}$. The *cis*-isomer showed two sharp absorptions, at 1093 and 1136 cm.$^{-1}$, and one of medium intensity at 781 cm.$^{-1}$. For calculation the pair at 1176 and 1093 cm.$^{-1}$ was chosen. The

TABLE 1.

Mixtures of known composition.

| *cis*-Isomer (%): | | | | | |
|---|---|---|---|---|---|
| exptl. | 15 | 30 | 50 | 72·5 | 83 |
| calc. | 16·6 | 27·75 | 50·2 | 72·5 | 85 |

TABLE 2.

Calculated isomer content in the different reaction products.

| Reaction | *cis*-Isomer (%) |
|---|---|
| Hydrogn. of (III) in neutral medium | 83 ± 2·5 |
| Hydrogn. of (III) in acidic medium | 43 ± 2·5 |
| Hydrogn. of (III) in alkaline medium | 42 ± 2·5 |
| Epimern. of mixture " A " with NaOMe for 3 hr. | 15 ± 2·5 |
| Epimern. of mixture " A " with NaOMe for 20 hr. | 13 ± 2·5 |
| Epimern. of mixture " A " on basic alumina overnight | 13 ± 2·5 |
| Epimern. of (XII) with NaOMe for 5 hr. | 14 ± 2·5 |
| Li–liq. $NH_3$ reduction of (III) | 21 ± 2·5 |
| Li–liq. $NH_3$ redn. of (III) in the presence of alcohol | 55 ± 2·5 |
| Epimern. of mixture " A " under the conditions of Li–liq. $NH_3$ reduction | 50 ± 2·5 |

isomer ratio of the epimeric *trans*-alcohols could be determined by using the two bands at 1000 and 1046 cm.$^{-1}$, characteristic of axial and equatorial alcohols, respectively. Calibration data for ketone mixtures of known composition are recorded in Table 1, and those obtained for different reaction mixtures in Table 2.

## EXPERIMENTAL

*γ-(2-Oxocycloheptyl)butyric Acid* (IV).—(*a*) Sodium (4·2 g.) was dissolved in absolute ethanol (53 ml.), and methyl 2-oxocycloheptanecarboxylate (20 g.) was added without heating. The mixture was stirred for 5 min., and methyl γ-bromobutyrate (35 g.) was added rapidly. The solution was then stirred and refluxed for 8 hr., cooled, poured into water (60 ml.), and extracted with ether. On distillation of the dried ($MgSO_4$) ether solution, an oil was formed, which was purified by distillation in a short-path still at 120—130°/0·01 mm. The distillate (15 g.) was refluxed in water (260 ml.) and methanol (125 ml.) containing barium hydroxide (40 g.) for 20 hr. The larger part of the methanol was then distilled off, the mixture acidified with concentrated hydrochloric acid, and the separated oil extracted with ether. The ether layer was washed several times with saturated sodium hydrogen carbonate solution, and the combined alkaline fractions were acidified with concentrated hydrochloric acid and re-extracted with ether. Evaporation of the dried ($MgSO_4$) ether solution gave an oil, which on distillation (138—140°/0·01 mm.) yielded the crude keto-acid (IV) (9·9 g.).

For purification this keto-acid (27 g.) was converted into its *semicarbazone* (33 g.), m. p. 177—179° (from methanol) (Found: C, 56·9; H, 8·0; O, 19·0; N, 16·5. $C_{12}H_{21}N_3O_3$ requires C, 56·45; H, 8·3; O, 18·8; N, 16·5%).

The semicarbazone (33 g.) was refluxed with oxalic acid (35 g.) in water (140 ml.) for 1 hr. The mixture was then cooled and extracted with ether, and the ether solution dried ($MgSO_4$). After removal of the solvent, distillation yielded the pure *keto-acid* (IV) (25 g.), b. p. 140—141°/0·01 mm., $n_D^{20}$ 1·4810 (Found: C, 66·5; H, 9·1; O, 25·0. $C_{11}H_{18}O_3$ requires C, 66·6; H, 9·15; O, 24·2%). The S-*benzylthiouronium salt* melted at 155—156° (from aqueous ethanol) (Found: C, 62·55; H, 7·65; O, 13·6; S, 9·0. $C_{19}H_{28}N_2O_3S$ requires C, 62·6; H, 7·7; O, 13·2; S, 8·8%).

(*b*) To a suspension of metallic potassium (9 g.) in dry benzene (150 ml.) methyl 2-oxocycloheptanecarboxylate (40 g.) was added dropwise during 0·5 hr. The reaction was exothermic and the solution became orange. Sodium iodide (0·8 g.) in absolute ethanol (4 ml.), followed

by methyl γ-bromobutyrate (42·5 g.) in dry benzene (70 ml.), was added dropwise and the mixture boiled and stirred for 38 hr. It was then poured on ice–salt, and the oil which separated was extracted with ether. From the dried ($MgSO_4$) ether solution a heavy oil was obtained, which was purified by distillation in a short-path still at 120—130°/0·01 mm. The product (63 g.) was hydrolysed and decarboxylated with barium hydroxide as described in (*a*), giving an oil (40 g.), which partially solidified on distillation at 140—144°/0·01 mm. Trituration with ether separated the oil (22 g.) from ether-insoluble crystals (16·5 g.). The solid was identified by its m. p., mixed m. p., and infrared spectrum as suberic acid. The oil was identical with the keto-acid (IV) obtained in method (*a*).

*γ-(2-Hydroxycycloheptyl)butyric Acid* (V; R = H).—To a methanol solution of the keto-acid (IV) (31·5 g.) sodium borohydride (10 g.) was added in small portions under cooling. The mixture was set aside overnight and the solvent evaporated under reduced pressure. Water and dilute hydrochloric acid were added and the mixture was extracted with ether. Drying ($MgSO_4$) and evaporation of the solvent gave a quantitative yield of the hydroxy-acid (V; R = H). The *S-benzylthiouronium salt* melted at 146—147° (from water) (Found: C, 61·9; H, 8·4; N, 7·7; S, 8·75. $C_{19}H_{30}N_2O_3S$ requires C, 62·3; H, 8·2; N, 7·65; S, 8·7%). The *3,5-dinitrobenzoate* had m. p. 88—89° (from ethanol) (Found: C, 54·8; H, 5·5; N, 7·2. $C_{18}H_{22}N_2O_8$ requires C, 54·8; H, 5·6; N, 7·1%).

*Methyl γ-(2-Hydroxycycloheptyl)butyrate* (V; R = Me).—The crude hydroxy-acid (V; R = H) (30 g.) was treated with an excess of ethereal diazomethane. The solution was kept for 2 hr. at room temperature (under the hood!), washed with sodium hydrogen carbonate solution, and water, and dried ($MgSO_4$). The *hydroxy-ester* (26 g.) had b. p. 108—110°/0·01 mm., $n_D^{20}$ 1·4815 (Found: C, 67·3; H, 10·6; O, 22·3. $C_{12}H_{22}O_3$ requires C, 67·25; H, 10·35; O, 22·4%), $\nu_{max.}$ (in $CHCl_3$) 3630, 3450, 1725 cm.$^{-1}$.

*Methyl γ-(Cyclohept-1-enyl)butyrate* (VI; R = Me).—(*a*) A solution of hydroxy-ester (V; R = Me) (2 g.) in dry benzene was shaken with phosphorus pentoxide (2 g.) overnight. Cold water (20 ml.) was then added and the mixture extracted with ether. The ether solution was washed with dilute sodium hydrogen carbonate solution and water and dried ($MgSO_4$). Evaporation gave the olefinic *ester* (1 g.), b. p. 67—70°/0·01 mm., $n_D^{18}$ 1·4700 (Found: C, 72·85; H, 10·3; O, 17·0. $C_{12}H_{20}O_2$ requires C, 73·4; H, 10·3; O, 16·3%), $\nu_{max.}$ (in $CHCl_3$) 1725 cm.$^{-1}$. It showed a strong positive test with tetranitromethane.

(*b*) The hydroxy-ester (V; R = Me) (8 g.) was dissolved in dry pyridine (15 ml.) and redistilled phosphorus oxychloride (6 g.) was added at 0°. The solution was set aside overnight at room temperature and then heated on a steam-bath for 1 hr. The mixture was cooled and decomposed with ice-water (20 ml.). The separated oil was extracted with ether, and the organic layer washed with dilute hydrochloric acid, sodium hydrogen carbonate solution, and water and dried on $MgSO_4$. After evaporation of the solvent, the olefinic ester (6·5 g.) was obtained, identical in properties and spectrum with that obtained in (*a*).

(*c*) The hydroxy-ester (V; R = Me) (8 g.) in dry pyridine (15 ml.) was treated overnight at room temperature with toluene-*p*-sulphonyl chloride (8 g.). The mixture was decomposed with ice-water (20 ml.) and worked up as usual. The crude dry toluene-*p*-sulphonate was refluxed in dry pyridine (40 ml.) for 2 hr. The cooled mixture was acidified with dilute sulphuric acid and extracted with ether–hexane. The olefinic ester (6 g.), obtained from the organic layer, was identical in its properties and spectrum with those obtained in (*a*) and (*b*).

The above ester (6·5 g.) was heated under reflux for 4 hr. with an excess of 15% aqueous potassium hydroxide. The cooled solution was acidified with dilute hydrochloric acid and extracted with ether. After the organic layer had been washed with water and dried ($MgSO_4$), the solvent was removed, and the residual oil distilled, yielding the pure olefinic *acid* (4·5 g.), b. p. 120—122°/0·01 mm., $n_D^{18}$ 1·4867 (Found: C, 72·3; H, 9·95; O, 16·7. $C_{11}H_{18}O_2$ requires C, 72·5; H, 9·95; O, 17·5%). The *S-benzylthiouronium salt* had m. p. 148—149° (from aqueous ethanol) (Found: C, 65·5; H, 7·8; N, 8·0; S, 9·25. $C_{19}H_{28}N_2O_2S$ requires C, 65·5; H, 8·0; N, 8·0; S, 9·2%).

*2,3,4,5,6,7,8,9-Octahydrobenzocyclohepten-1-one* (III).—In a three-necked flask redistilled acetic anhydride (1030 ml.), acetic acid (64 ml.) and a solution of freshly melted zinc chloride (1·28 g.) in acetic acid were mixed. The olefin acid (VI; R = H) (90 g.) was added dropwise and the mixture kept overnight under nitrogen. The solution was then boiled for 2 hr., concentrated under reduced pressure, diluted with ice-water, and extracted with ether. The extract was washed with sodium hydrogen carbonate solution, then water, dried ($MgSO_4$), and

evaporated, giving a crude oil (88 g.) which according to its infrared spectrum was a mixture of the unsaturated ketone and a lactone.

The crude oil was heated under reflux for 2 hr. with an excess of 10% sodium hydroxide solution. After the usual working up the crude oil (48 g.) showed only the infrared absorption of the unsaturated carbonyl group. From the acidified alkaline solution the acid (VI; R = H) (34 g.) was isolated.

The crude ketone (48 g.) was chromatographed in hexane on basic alumina (1900 g.; Fisher). Elution with hexane–benzene (3 : 1) gave a mobile oil (38 g.) which was distilled at 80—82°/0·01 mm. The ketone was finally purified by preparing its semicarbazone, which was smoothly cleaved by refluxing it with dilute oxalic acid. The ketone (III) has a terpene-like odour, b. p. 80°/0·01 mm., and $n_D^{25}$ 1·5265 (Found: C, 79·75; H, 9·7; O, 10·7. Calc. for $C_{11}H_{16}O$: C, 80·4; H, 9·8; O, 9·7%), $\nu_{max.}$ (in $CHCl_3$) 1650, 1625 cm.$^{-1}$, $\lambda_{max.}$ (in EtOH) 249, 308 mμ (log ε 4·112, 2·106 respectively). Repeating the purification did not improve the analytical results.

The deep-red 2,4-*dinitrophenylhydrazone* had m. p. 261—262° (from ethanol–chloroform) (Found: C, 59·2; H, 5·8; O, 18·6; N, 16·5. $C_{17}H_{20}N_4O_4$ requires C, 59·3; H, 5·85; O, 18·6; N, 16·3%). The *semicarbazone* (from aqueous methanol) melted at 206—207°(Found: C, 65·3; H, 8·3; O, 7·5; N, 18·9. $C_{12}H_{19}N_3O$ requires C, 65·1; H, 8·65; O, 7·2; N, 19·0%). The *oxime* had m. p. 148—149° (from aqueous methanol) (Found: C, 73·15; H, 9·35; O, 9·0; N, 7·8. $C_{11}H_{17}NO$ requires C, 73·7; H, 9·6; O, 8·9; N, 7·8%).

2,3,4,5,6,7,8,9-*Octahydrobenzocyclohepten*-1-*ol* (VII; R = H).—To a solution of ketone (III) (1 g.) in dry tetrahydrofuran (40 ml.) was added lithium hydridotri-t-butoxyaluminate (1·6 g.) under nitrogen, and the solution refluxed for 2 hr. The mixture was decomposed with Rochelle salt solution and extracted with ether. The oily residue (0·85 g.) obtained after removal of the solvent was chromatographed in pentane on basic alumina (35 g.; Fisher). Elution with pentane gave an unidentified mixture of cycloalkenes (0·12 g.), and with hexane–benzene (1 : 1) the solid allylic *alcohol* (0·38 g.), m. p. 55—56°, b. p. 100° (bath)/0·01 mm. (Found: C, 79·3; H, 10·7; O, 9·5. $C_{11}H_{18}O$ requires C, 79·5; H, 10·9; O, 9·6%).

The same compound was obtained on reduction with lithium aluminium hydride in dry ether.

The alcohol (1 g.), dry pyridine (4 ml.), and acetic anhydride (4 ml.) were kept together at room temperature overnight, giving an *acetate* (1·1 g.), b. p. 68—70°/0·2 mm., $n_D^{20}$ 1·4970 (Found: C, 74·8; H, 9·7; O, 15·5. $C_{13}H_{20}O_2$ requires C, 75·0; H, 9·7; O, 15·4%).

*Hydrolysis of the Acetate* (VII; R = Ac) *and Oxidation of the Resulting Alcohol* (VII; R = H).—The distilled acetate (0·8 g.) in 2% sodium methoxide solution was kept overnight at room temperature. After removal of the methanol, saturated sodium chloride (10 ml.) was added, and the oil taken up in ether. After drying ($MgSO_4$) and removal of the solvent, the allylic alcohol (0·63 g.) was obtained. The alcohol (0·6 g.) was shaken overnight with activated manganese dioxide [19] (4 g.) in carbon tetrachloride (10 ml.). The dried filtrate gave the crude unsaturated ketone (0·52 g.), which was purified by chromatography and successive distillation (b. p. 80°/0·01 mm.). The ketone was identical in its infrared spectrum as well as in m. p. of its derivatives with compound (III), described above.

*Catalytic Reduction of Compound* (III).—(a) *Neutral medium.* The unsaturated ketone (III) (2 g.) was hydrogenated in ethanol (100 ml.) in the presence of 10% palladised carbon (0·1 g.) at room temperature. After about 3 hr. 1 mol. of hydrogen had been taken up. Filtration and concentration of the filtrate under reduced pressure gave an oil (1·95 g.), b. p. 52—53°/0·01 mm. This was subjected to quantitative infrared analysis, which showed it to be a mixture (subsequently referred to as mixture " A ") of the *cis*- and *trans*-ketone (XII and XIII) containing 83 ± 2·5% of the former.

(b) *Acidic or basic medium.* A mixture of the unsaturated ketone (III) (0·25 g.), ethanol (10 ml.), 10% palladised carbon (0·05 g.), and 10% hydrochloric acid (1 ml.) or 10% sodium hydroxide solution (1 ml.) was hydrogenated at room temperature. After 1 mol. of hydrogen had been taken up (in the acidic medium after about 3 hr., in basic medium after about 2 days), the reaction stopped. Filtration and concentration gave an oil (0·24 g.), b. p. 53—54°/0·01 mm., shown by quantitative infrared analysis to contain about 43% of *cis*- and 57% of *trans*-ketone.

*Epimerisation of Mixture " A ".*—(a) *With sodium methoxide.* The mixture " A " (1 g.) in dry methanol (50 ml.) containing 10% sodium methoxide solution (3 ml.) was refluxed for 2 hr. The new equilibrium mixture (0·95 g.) was isolated by adding saturated sodium chloride

[19] Attenburrow, Cameron, Chapman, Evans, Hems, Jansen, and Walker, *J.*, 1952, 1094.

solution (20 ml.) after most of the methanol had been removed and subsequent ether-extraction; it had b. p. 60—61°/0·2 mm. The same reaction was repeated and the reaction time increased to 20 hr.

(b) *On basic alumina.* Mixture "A" (0·5 g.) in pentane was kept overnight on a column prepared from basic alumina (6 g.; Merck). The equilibrated ketone mixture was then eluted with pentane–ether (95 : 5), and had b. p. 60°/0·2 mm.

The infrared spectra of mixtures showed that in each case (a) and (b) 85—87% of the *trans*-epimer had been formed.

trans-*Perhydrobenzocyclohepten*-cis(eq)-1-*ol* [20] (XV) *and* -trans(ax)-1-*ol* [20] (XVI).—Epimerised (with sodium methoxide in methanol; see foregoing reaction), mixture "A" (2 g.) in dry tetrahydrofuran (80 ml.) was stirred overnight with lithium hydridotri-t-butoxyaluminate (5 g.) at 50°. The usual working-up (decomposition with Rochelle salt solution) gave the oily crude mixture (2 g.) of the saturated alcohols, which was purified by chromatography on basic alumina (80 g.; Alcoa) in hexane. Elution with hexane and increasing amounts (up to 30%) of methylene chloride separated the epimeric *trans*-alcohols, the axial being eluted before the equatorial epimer (total 1·7 g.). In the last fractions a minute amount of *cis*-alcohol (XIV) was eluted.

The trans-trans(ax)-*alcohol* (XVI) had b. p. 77—78°/0·5 mm., $n_D^{25}$ 1·5000 (Found: C, 78·3; H, 11·9; O, 9·6. $C_{11}H_{20}O$ requires C, 78·5; H, 12·0; O, 9·5%), $\nu_{max.}$ (in $CS_2$) 3640, 3500, 1000 cm.$^{-1}$. The p-*nitrobenzoate* had m. p. 70° (from methanol) (Found: C, 68·2; H, 7·2; O, 20·3; N, 4·5. $C_{18}H_{23}NO_4$ requires C, 68·1; H, 7·3; O, 20·2; N, 4·4%). The *acetate*, prepared by acetic anhydride in pyridine, had b. p. 59—60°/0·05 mm., $n_D^{20}$ 1·4792 (Found: C, 74·4; H, 10·6; O, 15·3. $C_{13}H_{22}O_2$ requires C, 74·2; H, 10·5; O, 15·2%), $\nu_{max.}$ (in $CS_2$) 1240 (composed), 1218 (shoulder), 1202 cm.$^{-1}$ (shoulder).

The trans-cis(eq)-*alcohol* (XV) had m. p. 56° (from pentane at liquid-air temperature) (Found: C, 78·3; H, 11·8; O, 9·7%), $\nu_{max.}$ (in $CS_2$) 3640, 3500, 1046 cm.$^{-1}$. The p-*nitrobenzoate* melted at 100—101° (from methanol) (Found: C, 68·1; H, 7·3; O, 20·3; N, 4·6%). The *acetate* had b. p. 63°/0·01 mm., $n_D^{25}$ 1·4780 (Found: C, 74·3; H, 10·3; O, 15·3%), $\nu_{max.}$ (in $CS_2$) 1240 cm.$^{-1}$.

When the epimeric *trans*-alcohols were eluted from the column (see above) without separation (in one fraction), the proportions of the equatorial and axial isomers was found to be 53 ± 2·5% and 47 ± 2·5% respectively.

cis-*Perhydrobenzocyclohepten*-1-*ol* (XIV).—Mixture "A" (1 g.) in dry ether (50 ml.) was added dropwise to a stirred and cooled slurry of lithium aluminium hydride (0·25 g.) in dry ether (50 ml.). After being stirred overnight at room temperature, the mixture was worked up as usual (with Rochelle salt). The crude mixture of isomeric alcohols (0·95 g.) was chromatographed in a minimum volume of pentane on alumina (40 g.; Alcoa). Elution was with a large volume of pentane–ether (95 : 5). The first fractions gave a mixture of *trans*-alcohols (XV, XVI) (0·12 g.) (identified by their infrared spectra and derivatives), followed by the pure cis-*alcohol* (0·6 g.), m. p. 60° (from pentane at liquid-air temperature) (Found: C, 78·4; H, 11·9; O, 9·7%), $\nu_{max.}$ (in $CS_2$) 3640, 3400, 1050, 1010 cm.$^{-1}$. The p-*nitrobenzoate* had m. p. 75° (from ethanol) (Found: C, 67·9; H, 7·3; O, 20·3; N, 4·6%). The *acetate* had b. p. 68°/0·02 mm., $n_D^{18}$ 1·4810 (Found: C, 74·5; H, 10·5; O, 15·4%), $\nu_{max.}$ (in $CS_2$) 1240, 1228 (shoulder), 1220 cm.$^{-1}$ (shoulder).

trans-*Perhydrobenzocyclohepten*-1-*one* (XIII).—The *trans*-alcohol (XVI) (0·6 g.) in pyridine (1 ml.) was added to the cooled chromic oxide–pyridine complex (from 0·6 g. of chromic oxide and 6 ml. pyridine), and the mixture kept overnight at room temperature. Ether and benzene were added and the suspension was filtered, washed with 10% acetic acid solution containing ferrous sulphate, then with water, 5% sodium hydrogen carbonate solution, and again with water, and dried ($MgSO_4$). On removal of the solvent the trans-*perhydrobenzocyclohepten*-1-*one* (XIII) was obtained in almost quantitative yield, with b. p. 55°/0·01 mm., $n_D^{20}$ 1·4948 (Found: C, 79·2; H, 10·7; O, 9·9. $C_{11}H_{18}O$ requires C, 79·5; H, 10·9; O, 9·6%), $\nu_{max.}$ (in $CS_2$) 1710, 1176, 913 cm.$^{-1}$. The 2,4-*dinitrophenylhydrazone* had m. p. 226° (from methanol–chloroform) (Found: C, 59·1; H, 6·3; N, 16·0. $C_{17}H_{22}N_4O_4$ requires C, 58·9; H, 6·4; N, 16·2%). The *semicarbazone* melted at 209—210° (from aqueous ethanol) (Found: C, 64·5; H, 9·1; N, 19·0. $C_{12}H_{21}N_3O$ requires C, 64·5; H, 9·5; N, 18·8%). The *oxime* had m. p. 141—142° (from ethanol) (Found: C, 73·0; H, 10·7; N, 7·7. $C_{11}H_{19}NO$ requires C, 72·9; H, 10·6; N, 7·7%).

[20] The *trans*-1 and *cis*-1 designation refer to the relation of the 1-substituent to the neighbouring hydrogen atom of the ring junction.

XUM

The same *trans*-ketone (XIII) was obtained when the alcohol (XV) was oxidised by the same method.

cis-*Perhydrobenzocyclohepten-1-one* (XII).—The *cis*-perhydrobenzocyclohepten-1-ol (XIV) was oxidised with the chromic oxide–pyridine complex as described for preparation of the *trans*-ketone (XIII), to give the cis-*ketone*, b. p. 53°/0·1 mm., $n_D^{20}$ 1·4959 (Found: C, 78·7; H, 10·9; O, 9·95%), $\nu_{max.}$ (in $CS_2$) 1706, 1093, 781 cm.$^{-1}$. The *semicarbazone* had m. p. 182—183° (from methanol) (Found: C, 64·4; H, 9·3; N, 18·6%). The *oxime* had m. p. 88—89° (from light petroleum) (Found: C, 72·7; H, 10·5; N, 7·9%).

Epimerisation of *cis*-ketone (XII) with sodium methoxide in methanol for 5 hr. (method described above for epimerisation of mixture " A ") gave a mixture containing 86% of the *trans*-isomer (XIII).

The semicarbazones of the saturated *cis*- and *trans*-ketones (XII and XIII respectively) behaved as homogeneous compounds, and known mixtures of them were readily separated when chromatographed on basic alumina.

*Reduction of Unsaturated Ketone* (III) *with Lithium in Liquid Ammonia.*—(*a*) The unsaturated ketone (III) (1 g.) in dry ether (5 ml.) was added to a mixture of lithium (0·1 g.) and liquid ammonia (500 ml.), prepared in a three-necked flask and cooled with acetone–solid carbon dioxide. After a few minutes more lithium (*ca.* 1·5 g.) was added in grain-sized pieces to the stirred solution until the blue colour persisted for 2 hr. The colour was then discharged by addition of solid ammonium chloride (*ca.* 1 g.). The ammonia was allowed to evaporate slowly and the residue taken up in water and extracted with ether. The ether solution was washed with dilute hydrochloric acid and then water, dried ($MgSO_4$), and evaporated. The resulting oil (0·85 g.) was shown to be a mixture of starting material and saturated ketones (XII and XIII). Separation in this stage was difficult; therefore the mixture was directly reduced by adding its ethereal solution (20 ml.) to a stirred and cooled slurry of lithium aluminium hydride (0·25 g.) in dry ether (20 ml.). The mixture was stirred at room temperature for 1 hr. and worked up on the usual way. The crude alcoholic product (0·8 g.) was chromatographed in pentane on basic alumina (35 g.; Alcoa). With a large volume of pentane–ether (9 : 1) the saturated alcohols (0·6 g.) were eluted before the unsaturated one (0·1 g.). The mixture of saturated alcohols was directly oxidised with the chromic oxide–pyridine complex as described above. The ketone mixture thus obtained was analysed by the infrared method and shown to contain 21 ± 2·5% of the *cis*- and 79 ± 2·5% of the *trans*-isomer.

(*b*) To a cooled (acetone–carbon dioxide) and stirred solution of lithium (2 g.) in liquid ammonia (500 ml.), absolute ethanol (10 ml.) was added, followed by a solution of the unsaturated ketone (III) (1 g.) in dry ether (5 ml.). Stirring was continued for 2 hr., ammonium chloride (1 g.) added, and the mixture worked up as described in (*a*). The oily product (0·65 g.) was chromatographed in pentane on basic alumina (30 g.; Alcoa). Elution with pentane–ether (9 : 1) gave a good separation between small amount of ketonic mixture (0·08 g.; partly starting material) and a mixture of saturated alcohols (0·5 g.). The alcohol mixture was oxidised with chromic oxide in pyridine, as described above, to give the mixture of saturated ketones (XII and XIII), containing 55 ± 2·5% of *cis*-isomer (estimated by the infrared method).

*Epimerisation of Mixture " A " with Lithium–Liquid Ammonia.*—To the stirred and cooled (acetone–carbon dioxide) mixture prepared by adding mixture " A " (0·25 g.) in dry ether (1 ml.) to liquid ammonia (100 ml.), lithium (0·2 g.) was added and the blue solution stirred for 2 hr. After the usual working up, the saturated ketone mixture was found by the infrared method to contain 50 ± 2·5% of *cis*-ketone.

*Measurement of Relative Oxidation Rates of Alcohols.*—These were kindly determined by Professor A. Eschenmoser and Mr. L. Moldovanyi at the Eidgenössiche Technische Hochschule, Zürich. The concentrations were $6·0 \times 10^{-4}$ mole/l. for the alcohols and $8·0 \times 10^{-4}$ mole/l for chromic oxide, in 90·5% acetic acid at 20° ± 1°. The rate constants (see Table 3) were calculated as described previously.[21]

TABLE 3.

Relative oxidation rates.

| Alcohol | *k* | Half-life (min.) | Suggested conformation |
|---|---|---|---|
| (XV) ..... | 1·9 | 63 | *eq* |
| (XVI) ..... | 5·1 | 18 | *ax* |

[21] Eschenmoser, *Helv. Chim. Acta*, 1955, **38**, 1529.

*Measurement of Relative Rates of Saponification of Acetates.*—The acetate (0·03 g.) was dissolved in 95% ethanol (5 ml.) and the volume was made up to 25·0 ml. with N/40-alcoholic sodium hydroxide. The solution was kept at 25·0° ± 1°, and 1·00 ml. portions were withdrawn at intervals and titrated with 0·01N-hydrochloric acid. The results, which were checked against a control solution, are shown in Table 4.

TABLE 4.

Relative hydrolysis rates.

(%) of the acetates saponified after (hr.)

| Alcohol | 2 | 5 | 12 | 24 | 29 | 36 | 48 | Suggested conformation |
|---|---|---|---|---|---|---|---|---|
| (XV) ..... | 6·5 | 15·5 | 32·75 | 49·15 | 62·25 | 73·75 | 82·0 | *eq* |
| (XVI) ..... | 0·0 | 0·0 | 0·0 | 0·9 | 7·15 | 11·75 | 16 | *ax* |

*Infrared Spectra.*—Measurements were made with a Perkin–Elmer model 21 spectrometer. In the quantitative analysis, the spectra of the ketones were measured at a total of 20·0 mg./10·50 ml. of $CS_2$ in 0·50 mm. cells, and those of the alcohols at 10·0 mg./0·50 ml. of $CS_2$ in 0·50 mm. cells.

*Nuclear Magnetic Resonance Spectra.*—The spectra were run at a frequency of 60 Mc./sec. on a Varian spectrometer model V-4300-c, and chemical shifts were determined by the side-band technique. The spectral sample consisted of 66·9 mg. of ketone in 0·6 ml. of deuterochloroform containing 2% of dissolved tetramethylsilane and was observed immediately after preparation in a thin-walled 5 mm. tube, while spinning.

The authors thank Professor David Ginsburg for his interest and encouragement, and Dr. Robert F. Hutton, Brandeis University, U.S.A., for determination and interpretation of the nuclear magnetic resonance spectra.

DEPARTMENT OF CHEMISTRY, TECHNION—ISRAEL INSTITUTE OF TECHNOLOGY,
HAIFA, ISRAEL. [*Received, June 8th,* 1961.]

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## 1055. *The Chemistry of Triterpenes and Related Compounds. Part XLI.* The Bromination of Lupeol and its Esters.*

By S. R. GUPTA, T. G. HALSALL, and E. R. H. JONES.

The confused literature on the bromination of lupeol and its derivatives is reviewed. Bromination of lupenyl acetate gives the side-chain monobromo-compounds, 29- and 30-bromo-20(29)-en-3β-yl acetates (VII) and (X). The allylic bromide is isomerised to the vinyl bromide by hydrobromic acid. On further treatment with hydrogen bromide, addition is accompanied by the expected skeletal rearrangement yielding 19α,29(or 30)-dibromo-18α-oleanan-3β-yl acetate (IV).

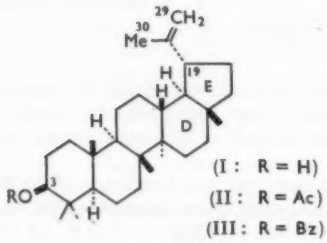
THE bromination of lupeol (I) and its derivatives has been studied by a number of workers, but the structures of the products have not been elucidated. In the early 1900's Cohen [1,2] treated lupeol with one mol. of bromine in carbon disulphide and in chloroform; hydrogen bromide was evolved, and he obtained a monobromo-derivative, $C_{30}H_{49}BrO$, m. p. 185°, $[\alpha]_D$ +4°. No dibromide was isolated. When lupenyl benzoate was brominated in a mixture of carbon disulphide and acetic acid two monobromo-derivatives were obtained. Separation was effected by taking advantage of their different solubilities in acetone. Only the constants of the less soluble product, m. p. 243°, $[\alpha]_D$ +45°, were recorded. Goodson [3]

* Part XL, *J.*, 1961, 3891.

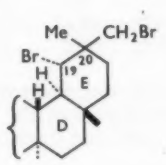
[1] Cohen, *Proc. k. Akad. Wetensch. Amsterdam*, 1906, **9**, 466.
[2] Cohen, *Rec. Trav. chim.*, 1909, **28**, 368.
[3] Goodson, *Biochem. J.*, 1921, **15**, 123.

later reported a monobromolupeol, m. p. 183°, and a monobromolupenyl acetate, m. p. 232°.

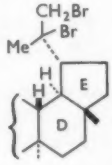
Subsequently the formation of a lupeol dibromide was reported. Dieterle [4] described such a product, m. p. 205—206° (decomp.), $[\alpha]_D$ +25°. Marker and Wittle [5] treated lupenyl acetate in ether with a slight excess of bromine in acetic acid and obtained a dibromide, m. p. 225° (decomp.). Similar treatment of lupeol yielded a dibromide, m. p. 186—190° (decomp.). Biedebach [6] also reported the isolation of lupenyl acetate dibromide, m. p. 225°, from the product of gradual addition of bromine in acetic acid to lupenyl



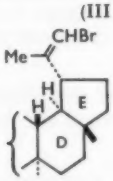
(I: R = H)
(II: R = Ac)
(III: R = Bz)



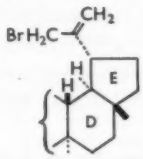
(IV)



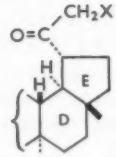
(V)



(VI; 3-OH)
(VII; 3-OAc)
(VIII; 3-OBz)



(IX; 3-OH)
(X; 3-OAc)
(XI; 3-OBz)



(XII; X = H)
(XIII; X = Br)

acetate in chloroform. When the dibromide was treated with silver nitrate in pyridine a product described as monobromolupenyl acetate, m. p. 205°, was isolated and hydrolysed to monobromolupeol, m. p. 196—197°.

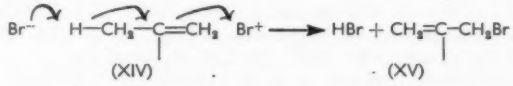
In view of these conflicting results a further investigation of the bromination of lupeol and its derivatives appeared desirable, more especially as, in the light of the known acid-catalysed rearrangements [7] of lupeol derivatives, it appeared possible that a dibromide might be formed by attack of $Br^+$ at $C_{(29)}$, rearrangement of the resulting carbonium ion, and attachment of $Br^-$ at $C_{(19)}$ of the rearranged ion, compound (IV) being formed. The only structure which has been proposed [8] for lupeol dibromide is (V).

Bromination of lupenyl acetate in the conditions used by Biedebach was first studied. His "dibromide," m. p. 225°, was not isolated. Instead two products were obtained. One was a monobromolupenyl acetate, m. p. 196—198°. The other was not homogeneous (see Experimental). The monobromo-derivative is 29-bromolupenyl acetate (VII), the structure being based on the following evidence. Reduction with sodium and isopropyl alcohol gave lupeol, and catalytic hydrogenation yielded lupanyl acetate. The carbon skeleton of lupeol is therefore present and ring enlargement has not occurred. On ozonolysis and treatment of the ozonide with boiling water the known norlupanonyl acetate [9] (XII) was isolated.

[4] Dieterle, *Arch. Pharm.*, 1923, **261**, 89, 97.
[5] Marker and Wittle, *J. Amer. Chem. Soc.*, 1939, **61**, 585.
[6] Biedebach, *Arch. Pharm.*, 1939, **277**, 163.
[7] Ames, Beton, Bowers, Halsall, and Jones, *J.*, 1954, 1905.
[8] Elsevier's "Encyclopaedia," Vol. XIV,S, p. 1122.
[9] Jones and Meakins, *J.*, 1940, 456.

When lupenyl acetate was brominated in ether at −78° two monobromolupenyl acetates were obtained. One was the 29-bromo-derivative (VII). The other, m. p. 235—236°, was shown to be the allylic bromo-compound, 30-bromolupenyl acetate (X). Reduction of the latter with sodium and isopropyl alcohol again gave lupeol, and hydrogenation lupanyl acetate. On ozonolysis formaldehyde was isolated as its dimethone. When the ozonide was reduced with zinc and acetic acid norlupanonyl acetate (XII), probably produced by reduction of an originally formed bromo-ketone, was again obtained. The ozonide was therefore decomposed in water at 100°, the bromoketo-acetate (XIII) being isolated.

The allylic bromide (X) was isomerised by hydrogen bromide in acetic acid–chloroform to the vinyl bromide (VII), but the reverse reaction did not occur (see below, however). The possibility therefore has to be considered that the allylic bromide is the first monobromo-product formed. It could arise from an initially formed, unstable dibromide, or be produced directly by the mechanism represented by (XIV ⟶ XV), this being akin to an $S_N2'$ substitution. The vinyl bromide (VII) could then arise by isomerisation of the initially formed allylic bromide (X). However, bromination of lupenyl acetate in propylene oxide, which should act as a proton acceptor,[10] afforded only the vinyl bromide (VII). An alternative explanation of the results is that the two bromides are produced independently by distinct reactions.



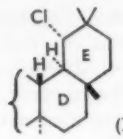

Similar results were obtained with lupenyl benzoate (III). When propylene oxide was used as solvent, only the vinyl bromide (VIII) was obtained. Its identity was established by comparison with the benzoate obtained from 29-bromolupeol (VI) which had been prepared from 29-bromolupenyl acetate. Bromination of lupenyl benzoate in ether gave a mixture of the vinyl (VIII) and allylic (XI) bromide. The latter was also prepared by benzoylation of 30-bromolupeol (IX).

The constants of 30-bromolupeol, m. p. 188—189°, $[\alpha]_D$ +2°, are very similar to those of Cohen's "monobromolupeol,"[1,2] m. p. 185°, $[\alpha]_D$ +4°. The absence of specific rotations for most of the other earlier bromination products makes comparison impossible.

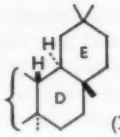
Biedebach[11] reported that "monobromolupeol" in boiling acetic anhydride was converted to a small extent into a compound which had the same melting point as γ-allolupenyl acetate (germanicyl acetate)[12] but with which he said it was not identical. In our work only starting material was recovered when 29-bromolupenyl acetate (VII) was heated under reflux in acetic anhydride. Silver acetate also failed to react with the acetate, thus confirming that the bromine atom attached to $C_{(29)}$ in the acetate (VII) is extremely unreactive.

Lupenyl acetate with hydrogen chloride gives[13] the "hydrochloride" (XVI) (19α-chloro-18α-oleanan-3β-yl acetate) which can be converted back into lupenyl acetate with silver acetate. When 29-bromolupenyl acetate (VII) was treated with hydrogen bromide a similar rearrangement accompanied addition of the hydrogen bromide and 19α,29(or 30)-dibromo-18α-oleananyl acetate (IV) was obtained. The structure, apart from the configuration at position 20, follows from the reduction of the dibromo-compound with sodium and isopropyl alcohol to the known 18α-oleanan-3β-ol [isolated as its acetate[14] (XVII)] and by its conversion back into 29-bromolupenyl acetate by silver acetate.

[10] Kirk, Patel, and Petrow, *J.*, 1956, 627.
[11] Biedebach, *Arch. Pharm.*, 1943, **281**, 49.
[12] Halsall, Jones, and Swayne, *J.*, 1954, 1902.
[13] Halsall, Jones, and Meakins, *J.*, 1952, 2862.
[14] Budziarek, Manson, and Spring, *J.*, 1951, 741.




(XVI)




(XVII)

The constants of the earlier bromination products and of the bromo-derivatives now prepared are given in the Table in the Experimental section.

## Experimental

Rotations refer to solutions in chloroform at room temperature. M. p.s were determined on a Kofler block and are corrected. The alumina used for chromatography (unless otherwise stated) was alumina of activity I—II which had been deactivated with 5% of 10% aqueous acetic acid. Light petroleum refers to the fraction with b. p. 60—80°. Unless otherwise stated, ultraviolet spectra were determined for n-hexane solutions.

*Bromination of Lupenyl Acetate* (II).—(*a*) Bromine (0·36 g., 1·05 mol.) in acetic acid (5 c.c.) was added in 15 min. to lupenyl acetate (1·0 g.) in chloroform (6 c.c.) at 0°. After acetic acid (10 c.c.) had been added the mixture was kept in the dark at 20° overnight. The mixture was concentrated under reduced pressure and cooled, a product (0·85 g.) separating. This was filtered off, washed with acetic acid, dried, and adsorbed from light petroleum (75 c.c.) on alumina (50 g.). Elution with the solvents indicated gave the following fractions: (1—3) light petroleum (L.P.) (350 c.c.), 235 mg., m. p. 190—195°; (4) L.P. (50 c.c.), 89 mg., m. p. 190—202°; (5) L.P.–benzene (B.) (9 : 1) (50 c.c.), 89 mg., m. p. 195—210°; (6—7) L.P.–B. (9 : 1) (250 c.c.), 165 mg., m. p. 200—220°; (8) L.P.–B. (9 : 1) (50 c.c.), 64 mg., m. p. 214—230°; (9) L.P.–B. (1 : 1) (50 c.c.), 45 mg., m. p. 225—240°; (10) L.P.–B. (1 : 1) (50 c.c.), 33 mg., m. p. 234—243°; (11) L.P.–B. (1 : 1) (50 c.c.), 8 mg., m. p. 242—245°.

Fractions (1—3) were recrystallised from chloroform–methanol to give 29-*bromolup*-20(29)-*en*-3β-*yl acetate* (VII) as needles, m. p. 196—198°, $[\alpha]_D$ +30° (*c* 1·32) (Found: C, 70·0; H, 9·0; Br, 14·9. $C_{32}H_{51}BrO_2$ requires C, 70·2; H, 9·3; Br, 14·6%).

Fractions (9—11) were combined and adsorbed from light petroleum (50 c.c.) on alumina (30 g.). The product obtained by elution with light petroleum–benzene (1 : 1) crystallised from chloroform–methanol as plates (48 mg.), m. p. 250—252°, $[\alpha]_D$ −46° (*c* 1·23) (Found: C, 54·7; H, 7·2; Br, 32·0. Calc. for $C_{32}H_{51}Br_3O_2$: C, 54·3; H, 7·2; Br, 33·9%). This material was shown to be inhomogeneous (see later).

Additional quantities of 29-bromolup-20(29)-en-3β-yl acetate (250 mg.), m. p. 194—198°, and the tribromo-product (11 mg.), m. p. 250—252°, were obtained by further chromatography of the middle fractions.

(*b*) Lupenyl acetate (1·0 g.) in ether (50 c.c.) at −78° was treated with bromine (0·375 g., 1·1 mol.) in ether (50 c.c.) during 45 min. The light yellow mixture was then kept overnight at 20°. The solvent was removed and the residue was thrice crystallised from chloroform–methanol, to give 30-*bromolup*-20(29)-*en*-3β-*yl acetate* (X) as prisms (510 mg.), m. p. 235—236°, $[\alpha]_D$ +11° (*c* 1·34) (Found: C, 70·6; H, 9·2; Br, 14·35. $C_{32}H_{51}BrO_2$ requires C, 70·2; H, 9·3; Br, 14·6%).

The material (400 mg.) recovered from the mother liquors was adsorbed from light petroleum (75 c.c.) on alumina (50 g.). The fractions (128 mg.) obtained by elution with light petroleum (450 c.c.) had m. p. 192—195°. They crystallised from chloroform–methanol to give 29-bromolup-20(29)-en-3β-yl acetate (VII) as needles, m. p. and mixed m. p. 196—198°, $[\alpha]_D$ +30° (*c* 1·23).

(*c*) Lupenyl acetate (0·5 g.) in propylene oxide (100 c.c.) at −30° was treated with bromine (0·18 g., 1·05 mol.) in acetic acid (5 c.c.) during 30 min. The mixture was kept in the dark at 20° overnight, then diluted with water, and the precipitated solid was extracted with ether. The extract afforded 29-bromolup-20(29)-en-3β-yl acetate (VII) as needles (from chloroform–methanol) (280 mg.), m. p. and mixed m. p. 195—196°, $[\alpha]_D$ +30° (*c* 1·2).

*Attempted Isomerisation of* 29-*Bromolup*-20(29)-*en*-3β-*yl Acetate* (VII).—The acetate (0·5 g.), m. p. 196—198°, in chloroform (2 c.c.) was treated with hydrobromic acid (0·3 c.c.; 50% w/v in acetic acid) in acetic acid (5 c.c.) at 20° for 24 hr. The product (0·46 g.) was isolated in the usual manner. After two crystallisations from chloroform–methanol it afforded starting material, m. p. and mixed m. p. 193—195°, $[\alpha]_D$ +31° (*c* 1·2).

*Reduction of* 29-*Bromolup*-20(29)-*en*-3β-*yl Acetate* (VII) *with Sodium and Isopropyl Alcohol.*—Sodium (7 g.) was added in small pieces during 3 hr. to a boiling solution of the acetate (0·25 g.) in isopropyl alcohol (50 c.c.). After destruction of the excess of sodium with ethanol and dilution with water, extraction with chloroform afforded a product which was crystallised from chloroform–methanol to give lupeol (I) as needles, m. p. and mixed m. p. 211—213°, $[\alpha]_D$ +29° (*c* 1·1).

*Hydrogenation of* 29-*Bromolup*-20(29)-*en*-3β-*yl Acetate* (VII).—The acetate (0·29 g.) in ethanol (75 c.c.) was hydrogenated in the presence of Adams catalyst (110 mg.) for 11 hr. After removal of the catalyst, concentration of the solution afforded lupanyl acetate (0·21 g.), m. p. and mixed m. p. 241—242°, $[\alpha]_D$ +1° (*c* 1·8).

*Ozonolysis of* 29-*Bromolup*-20(29)-*en*-3β-*yl Acetate* (VII).—The acetate (130 mg.) in ethyl acetate (50 c.c.) at −78° was treated with ozonised oxygen (6%) until the solution became faintly blue (25 min.). Nitrogen was then bubbled through the solution and the mixture then washed twice with water. The solvent was removed and the residue was heated with water (150 c.c.) for 1·5 hr. The product (83 mg.) was adsorbed from light petroleum on alumina (20 g.). Elution with light petroleum afforded 3β-acetoxy-30-norlupan-20-one (XII) as plates (49 mg.) (from chloroform–methanol), m. p. and mixed m. p. 260—262°.

29-*Bromolup*-20(29)-*en*-3β-*ol* (VI).—The corresponding acetate (1·0 g.) was dissolved in benzene (80 c.c.) and ether (80 c.c.). Powdered lithium aluminium hydride (500 mg.) was added with shaking and the mixture heated under reflux for 30 min. The product crystallised from light petroleum and then from methanol, affording 29-*bromolup*-20(29)-*en*-3β-*ol* (VI) as needles (820 mg.), m. p. 180—182°, $[\alpha]_D$ +18° (*c* 1·42) (Found: C, 71·6; H, 9·7. $C_{30}H_{49}BrO$ requires C, 71·3; H, 9·7%).

Hydrolysis of the acetate (1 g.) with boiling 3% ethanolic potassium hydroxide (60 c.c.) for 40 min. afforded the same alcohol, m. p. 180—182°, $[\alpha]_D$ +34° (*c* 0·9) (Found: C, 71·35; H, 9·8%).

The alcohol (230 mg.) was treated with benzoyl chloride (3 c.c.) and pyridine (5 c.c.) at 100° for 1 hr., to give 29-*bromo*-20(29)-*en*-3β-*yl benzoate* (VIII) as plates (from methanol–chloroform), m. p. 234—236°, $[\alpha]_D$ +54° (*c* 1·75) (Found: C, 73·0; H, 8·75; Br, 12·95. $C_{37}H_{53}BrO_2$ requires C, 72·75; H, 8·7; Br, 13·15%).

*Isomerisation of* 30-*Bromolup*-20(29)-*en*-3β-*yl Acetate* (X).—The acetate (200 mg.) in chloroform–acetic acid (1 : 1; 10 c.c.) was treated with hydrobromic acid (1 c.c.; 50% w/v in acetic acid) for 24 hr. The product (190 mg.) was adsorbed from light petroleum (25 c.c.) on alumina (20 g.) and eluted with light petroleum. The fraction (110 mg.) obtained with the first 50 c.c. of eluent had m. p. 187—192°. It crystallised from ethanol, to give 29-bromolup-20(29)-en-3β-yl acetate as needles, m. p. and mixed m. p. 196—198°, $[\alpha]_D$ +30° (*c* 1·2). More of the 29-bromo-derivative (40 mg.) was obtained from later fractions from the chromatogram.

*Reduction of* 30-*Bromolup*-20(29)-*en*-3β-*yl Acetate* (X) *with Sodium and Isopropyl Alcohol.*—To a boiling solution of the acetate (1 g.) in isopropyl alcohol (200 c.c.) were added small pieces of sodium (22—23 g.) in 4 hr. The excess of sodium was destroyed with ethanol, and the solution was diluted with water. Extraction with chloroform afforded a product which was purified by percolation through alumina (50 g.) in light petroleum to give lupeol (560 mg.) as needles, m. p. and mixed m. p. 208—212°. Acetylation afforded lupenyl acetate, m. p. and mixed m. p. 215—217°.

*Hydrogenation of* 30-*Bromolup*-20(29)-*en*-3β-*yl Acetate* (X).—The acetate (247 mg.) in ethanol (150 c.c.) was completely hydrogenated in 4 hr. in the presence of Adams catalyst (100 mg.). After the catalyst had been removed the solution was concentrated to afford lupanyl acetate (172 mg.), m. p. and mixed m. p. 239—241°, $[\alpha]_D$ +3° (*c* 1·40) (Found: C, 81·3; H, 11·2. Calc. for $C_{32}H_{52}O_2$: C, 81·7; H, 11·5%).

*Ozonolysis of* 30-*Bromolup*-20(29)-*en*-3β-*yl Acetate.*—The acetate (182 mg.) in ethyl acetate (75 c.c.) was treated with ozonised oxygen (6%) until the solution became slightly bluish (16 min.). The mixture was treated with zinc and acetic acid and then steam distilled until 350 c.c. of distillate had been collected. The distillate afforded formaldehyde dimethone (24 mg., 25%), m. p. and mixed m. p. 189°. The ketone remaining after distillation was isolated, purified by chromatography on alumina, and crystallised from chloroform–methanol, to give 3β-acetoxy-30-norlupan-20-one (XII) as plates, m. p. and mixed m. p. 260—262°.

In a second experiment the acetate (320 mg.) in ethyl acetate (75 c.c.) was ozonised. The excess of ozone was then expelled with nitrogen. The solvent was removed and the residue

XUM

heated with water (150 c.c.) for 1·5 hr., giving a product (234 mg.) that was adsorbed from light petroleum on alumina (30 g.). The fractions obtained by elution with light petroleum–benzene (9 : 1) crystallised from ethanol, to give 3β-*acetoxy*-29-*bromo*-30-*norlupan*-20-*one* (XIII) as plates, m. p. 207—210° (Found: C, 67·5; H, 8·6. $C_{31}H_{49}BrO_3$ requires C, 67·75; H, 8·9%).

30-*Bromolup*-20(29)-*en*-3β-*yl Benzoate* (XI).—30-Bromolup-20(29)-en-3β-yl acetate (X) (1·30 g.) was dissolved in ether (700 c.c.); powdered lithium aluminium hydride (900 mg.) was added with shaking and then the mixture was boiled under reflux for 30 min. The product afforded 30-bromolup-20(29)-en-3β-ol (IX) as needles (from ethanol) (910 mg.), m. p. 188—189°, $[\alpha]_D$ +2° (*c* 1·2). The alcohol (280 mg.) was treated with benzoyl chloride (2 c.c.) and pyridine (3 c.c.) at 100° for 3 hr. to give 30-*bromolup*-20(29)-*en*-3β-*yl benzoate* as plates (from chloroform–methanol), m. p. 251—252°, $[\alpha]_D$ +56° (*c* 1·2) (Found: C, 72·3; H, 8·7; Br, 12·9. $C_{37}H_{53}BrO_2$ requires C, 72·75; H, 8·7; Br, 13·15%).

*Bromination of Lupenyl Benzoate in Propylene Oxide.*—Lupenyl benzoate (500 mg.) in propylene oxide (75 c.c.) was treated with bromine (0·18 g., 1·05 mol.) in acetic acid (5 c.c.) during 15 min. The mixture was kept for 15 min. and then diluted with water. The precipitate (400 mg.) was collected, washed, and dried. It was adsorbed from light petroleum (75 c.c.) on alumina (50 g.). Elution with light petroleum afforded 29-bromolup-20(29)-en-3β-yl benzoate (VIII) as plates (190 mg.) (from chloroform–methanol), m. p. and mixed m. p. 234—236°; $[\alpha]_D$ +54°.

*Bromination of Lupenyl Benzoate in Ether.*—The benzoate (590 mg.) in ether (150 c.c.) was treated with bromine (1·2 mol.) in ether (50 c.c.) during 25 min. The solution was kept for 8 hr. at 20°. Removal of the ether by distillation afforded a product which crystallised from chloroform–methanol to give 30-bromolup-20(29)-en-3β-yl benzoate (XI) as plates, m. p. and mixed m. p. 249—250°, $[\alpha]_D$ +54° (*c* 1·25).

*Reduction of the Bromination Product, m. p.* 250—252°.—Sodium (*ca.* 8 g.) in small pieces was added gradually during 2 hr. to a boiling solution of the bromination product, m. p. 250—252° (300 mg.), in isopropyl alcohol (60 c.c.). The reduction product (150 mg.), m. p. 165—190°, with pyridine and acetic anhydride at 100° gave a product (90 mg.), m. p. 244—246°, $[\alpha]_D$ +44° (*c* 0·8). This (70 mg.) was adsorbed from light petroleum (b. p. 38°) on alumina (70 g.) and eluted with light petroleum. The first fraction (23 mg.) had m. p. 275—278°. Recrystallisation from chloroform–methanol gave 18α-oleanan-3β-yl acetate (XVII) as plates, m. p. and mixed m. p. 280—282°. The last fraction (fourth) gave crystals (8 mg.), m. p. 229—232°, $[\alpha]_D$ +29° (*c* 0·9). The acetate (XVII) most likely arises from 19α,29,29(or 30,30)-tribromo-18α-oleanan-3β-yl acetate.

*Action of Hydrobromic Acid on* 29-*Bromolup*-20(29)-*en*-3β-*yl Acetate* (VII).—The acetate (1 g.) in acetic acid (75 c.c.) was treated with hydrobromic acid (50% w/v in acetic acid) (20 c.c.) at 20° and the solution was kept in the dark for 48 hr. Dilution of the reaction mixture with water (500 c.c.) gave a precipitate (0·86 g.) which was collected and washed with water. Crystallisation from ethanol and from chloroform–ethanol gave 19α,29(or 30)-*dibromo*-18α-*oleanan*-3β-*yl acetate* (IV) as plates (100 mg.), m. p. 235—236°, $[\alpha]_D$ −4° (*c* 1·0) (Found: C, 60·9; H, 8·3; Br, 23·5. $C_{32}H_{52}Br_2O_2$ requires C, 61·15; H, 8·3; Br, 25·5%). The mother liquors yielded starting material (250 mg.).

*Reduction of* 19α,29(*or* 30)-*Dibromo*-18α-*oleanan*-3β-*yl Acetate* (IV) *with Sodium and Isopropyl Alcohol.*—Sodium (*ca.* 6 g.) was added in small pieces during 2 hr. to a boiling solution of the acetate (230 mg.) in isopropyl alcohol (30 c.c.). The product (150 mg.) was treated at 100° for 2 hr. with pyridine and acetic anhydride, and the acetate adsorbed from light petroleum on alumina (20 g.). Elution with light petroleum (500 c.c.) yielded 18α-oleanan-3β-yl acetate (XVII) as plates (30 mg.) (from chloroform–methanol), m. p. and mixed m. p. 278—282°, $[\alpha]_D$ +39° (Found: C, 81·5; H, 11·55. Calc. for $C_{32}H_{54}O_2$: C, 81·65; H, 11·6%).

*Action of Acetic Anhydride on* 29-*Bromolup*-20(29)-*en*-3β-*yl Acetate.*—The acetate (1·0 g.) in acetic anhydride (25 c.c.) was heated under reflux for 22 hr. The anhydride was distilled off and the residue macerated with ice to decompose any anhydride. The product (0·98 g.) was purified by percolation through alumina. The resulting solid crystallised from chloroform–methanol to give starting material as needles (0·81 g.), m. p. and mixed m. p. 193—195°, $[\alpha]_D$ +30° (*c* 1·2).

*Action of Silver Acetate on* 19α,29(*or* 30)-*Dibromo*-18α-*oleanan*-3β-*yl Acetate* (IV).—The acetate (450 mg.) in ethanol (50 c.c.) was heated under reflux with silver acetate (800 mg.) for 20 hr. During this period the suspended solid became dark and a silver mirror formed on the surface

of the flask. Dilution with water and extraction with ether afforded a product which was heated with acetic anhydride (10 c.c.) for 30 min. The solution was poured into water and extracted with ether. The product crystallised from chloroform–methanol to give 29-bromolup-20(29)-en-3β-yl acetate (VII) as needles (230 mg.), m. p. and mixed m. p. 195—196°, $[\alpha]_D$ +30° (*c* 1·2).

Constants of bromination products.

| Product | M. p. | $[\alpha]_D$ | Ref. |
|---|---|---|---|
| " Monobromolupeol " | 185° | +4° | 1, 2 |
| " Monobromolupeol " | 183 | — | 3 |
| " Monobromolupeol " | 196—197 | — | 6 |
| 29-Bromolup-20(29)-en-3β-ol (VI) | 180—182 | +18(24) | This paper |
| 30-Bromolup-20(29)-en-3β-ol (IX) | 188—189 | +2 | This paper |
| " Monobromolupenyl acetate " | 232 | — | 3 |
| " Monobromolupenyl acetate " | 197—205 | — | 6 |
| 29-Bromolup-20(29)-en-3β-yl acetate (VII) | 196—198 | +30 | This paper |
| 30-Bromolup-20(29)-en-3β-yl acetate (X) | 235—236 | +11 | This paper |
| " Monobromolupenyl benzoate " | 243 | +45 | 1, 2 |
| " Monobromolupenyl benzoate " | — | — | 1, 2 |
| 29-Bromolup-20(29)-en-3β-yl benzoate (VIII) | 234—236 | +54 | This paper |
| 30-Bromo-20(29)-en-3β-yl benzoate (XI) | 251—252 | +56 | This paper |
| " Lupeol dibromide " | 205—206 | +25 | 4 |
| " Lupeol dibromide " | 186—189 | — | 5 |
| " Lupenyl acetate dibromide " | 225 | — | 5 |
| " Lupenyl acetate dibromide " | 225 | — | 6 |
| 19α,29(or 30)-Dibromo-18α-oleanan-3β-yl acetate | 235—236 | −4 | This paper |

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## 1056. *Carbonic Esters of Sucrose. Part I. The Preparation of O-Alkyloxycarbonylsucroses.*

By R. S. THEOBALD.

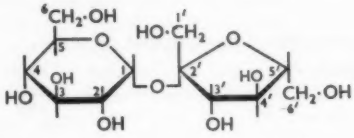
Sucrose reacts with alkyl chloroformates at 0° in the presence of aqueous alkali, yielding incompletely substituted *O*-alkyloxycarbonyl derivatives. Partial separation of the mixed esters is achieved by chromatography on papers impregnated with dimethyl sulphoxide as the stationary phase. Crystalline octa-*O*-ethoxycarbonylsucrose has been prepared by further acylation in pyridine. The more highly substituted *O*-alkyloxycarbonylsucroses show unusual stability to acid. An approximately trisubstituted *O*-ethoxycarbonylsucrose polymerises when heated.

THE " bridging " of the two hexose residues of sucrose (I), an acid-labile disaccharide, with bivalent atoms or small radicals, as for example methylenedioxy and carbonate, was attempted in order to retain the two monosaccharides in combination with one another after hydrolysis of the hemiacetal linkage. By this means it was hoped to prepare new long-chain polyhydric alcohols bearing two reducing groups. Only one example of a bridged sucrose derivative is known, the 1′,2:3,6:3′,6′-trianhydro-compound obtained by Lemieux and Barrette.[1]

The use of methylene sulphate to prepare cyclic methylene ethers of *ortho*-dihydric phenols and glycols has been reported,[2] but under the alkaline reaction conditions required for sucrose this reagent was without effect upon the carbohydrate. With molecular models, strainless carbonate bridges may be constructed between, for example, positions

[1] Lemieux and Barrette, *Canad. J. Chem.*, 1959, **37**, 1964.
[2] Baker, *J.*, 1931, 1765.

6,6′; 6,1′; 2,6′; and 2,1′ of sucrose. Whilst no evidence of such bridging has been obtained experimentally, the properties of the carbonic esters prepared in the investigation have proved of interest.




(I)

Hochstetter [3] in 1912 obtained an amorphous uncharacterised "carbonate" by the action of diphenyl carbonate on sucrose in molten resorcinol at 130°. Allpress and Haworth,[4] treating sucrose in pyridine at 0° with methyl chloroformate, synthesised a "hepta- or octa-" *O*-methoxycarbonyl derivative in low yield. Their glassy product corresponds more closely in analysis to a hexasubstituted ester, but was probably not homogeneous. The addition-polymerisation of octa-*O*-allyloxycarbonylsucrose was examined by Zief [5] in 1950.

Although Allpress and Haworth [4] appear to have originated the use of aqueous alkali as an acid-acceptor in chloroformate reactions upon carbohydrates, they did not apply this method to sucrose. It has now been found that high yields of *O*-alkyloxycarbonylsucroses result from the slow addition of 2N-sodium hydroxide to a well-stirred mixture of concentrated aqueous sucrose with an alkyl chloroformate at 0°. The precipitated syrups comprise esters at various stages of substitution and also isomers of the same degree of substitution (D.S.). An indication of the complexity of the mixtures was afforded by paper chromatography with an organic two-phase solvent system, a technique employed by Wickberg [6] for the separation of sugar acetates: the choice of a polar solvent for the stationary phase may be critical for a particular ester mixture; an *O*-methoxycarbonylsucrose (D.S. 6·8) appeared to consist of only three components when subjected to chromatography on a dimethyl sulphoxide-treated paper, but was separated into at least eight components when formamide was used. Whilst the preparative separation of individual *O*-alkyloxycarbonylsucroses has not yet been attempted, a partial solvent-fractionation is possible in some cases, and such fractions are suitable for many purposes (see below).

The introduction of five-membered cyclic carbonate groups into sucrose is theoretically impossible owing to the lack of *cis*-adjacent hydroxyl groups,[7] and their absence in these esters was confirmed by the single C=O stretching maximum, in the range 1754—1760 cm.$^{-1}$, observed in the infrared absorption spectra.[8] Comparison of the methoxyl value (micro-Zeisel) of an *O*-methoxycarbonylsucrose with the total carbonate content, estimated after alkaline hydrolysis, indicated that only *O*-methoxycarbonyl groups were present. The average degrees of substitution of various *O*-alkyloxycarbonylsucroses, prepared by using 10 mol. each of alkyl chloroformate and sodium hydroxide per mol. of sucrose, are listed in the Table. A difunctional chloroformic ester can lead to polymer formation. Thus, from sucrose, ethylene dichloroformate, and sodium hydroxide was obtained about 30% of an amorphous insoluble polycarbonate.

Except in the case of benzyl chloroformate, complete (octa)substitution of sucrose was not achieved by the chloroformic ester–aqueous alkali method, even with a large molar excess of reagents: 50 mol. each of methyl chloroformate and sodium hydroxide introduced only an average of 6·8 ester groups. This resistance is probably connected with

[3] Hochstetter, G.P. 268,452/1912 (*Friedländer*, 1913, **11**, 1211).
[4] Allpress and Haworth, *J.*, 1924, **125**, 1223.
[5] Zief, *J. Amer. Chem. Soc.*, 1950, **72**, 1137.
[6] Wickberg, *Acta Chem. Scand.*, 1958, **12**, 615.
[7] Hough, Priddle, and Theobald, *Adv. Carbohydrate Chem.*, 1960, **15**, 101.
[8] Hough, Priddle, Theobald, Barker, Douglas, and Spoors, *Chem. and Ind.*, 1960, 148.

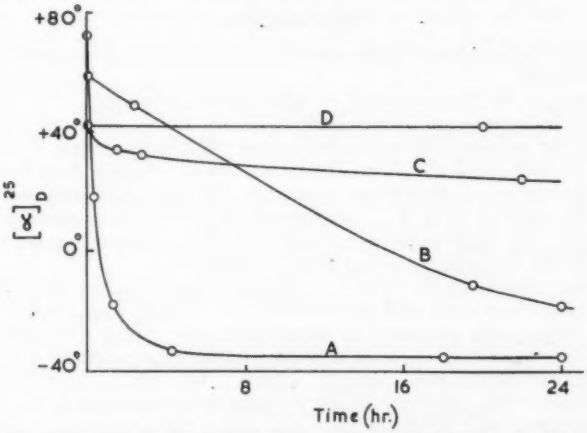
the alkali-lability of the *O*-alkyloxycarbonyl group.[4] A crystalline octa-*O*-ethoxycarbonylsucrose was, however, readily prepared by treating the partly esterified derivative (D.S. 5·7) with an excess of ethyl chloroformate in pyridine, further evidence that no carbonate bridges were present in the starting material.

*O*-Alkyloxycarbonylsucroses, $C_{12}H_{22-n}O_{11}(CO{\cdot}OR)_n$.

| R | Yield (%) (based on sucrose) | Found (%) C | H | OR | *n* (calc. from % OR) [c] | $[\alpha]_D^{25}$ (*c* in EtOH) | $\nu_{max.}$ (cm.$^{-1}$) (C=O stretching) [b] |
|---|---|---|---|---|---|---|---|
| Me ..... | 76 | 41·5 | 5·4 | 24·1 | 4·9 | +50·6° (4·34) | 1760 |
| Et ..... | 86 | 45·9 | 6·3 | 31·9 | 4·9 | +43·6 (5·55) | 1760 |
| Pr ..... | 87 | 49·4 | 7·0 | 38·1 | 5·0 | +37·3 (3·84) | 1755 |
| Pr$^i$ ..... | 90 | 50·2 | 7·0 | 39·5 | 6·0 | +37·5 (1·68) | 1754 |
| Bu ..... | 92 | 53·2 | 7·5 | 43·3 | 5·0 | +33·3 (6·04) | 1760 |
| Bu$^i$ ..... | 89 | 53·7 | 7·4 | 45·1 | 5·5 | +29·5 (5·51) | — |
| Bu$^s$ ..... | 70 | 53·9 | 7·0 | 46·5 | 6·0 | +31·5 (4·52) | 1754 |
| $CH_2Ph$ ..... | 79 | 64·9 | 4·7 | — | 8·0 [a] | +21·2 (2·04 [d]) | 1760 |

[a] Calc. from C,H values. [b] Determined on Unicam S.P. 100 double-beam infrared spectrometer with a rock-salt prism; evaporated film, ($CHCl_3$). [c] Variation of C,H with *n* is small, especially for lower members. [d] In $CHCl_3$.

The *O*-alkyloxycarbonylsucroses listed in the Table were colourless syrups at room temperature, increasing slightly in mobility with increasing size of the alkyl group. Although only sparingly soluble in water, they dissolved in most common organic solvents except light petroleum. As with organic carbonates in general, alkaline hydrolysis




Hydrolysis of sucrose and its esters in N-aqueous-alcoholic hydrochloric acid.
(A) Sucrose. (B) Sucrose octa-acetate. (C) *O*-Ethoxycarbonylsucrose (D.S. 3·1). (D) *O*-Ethoxycarbonylsucrose (D.S. 4·9).

occurred easily. Aqueous-alcoholic barium hydroxide rapidly yielded a precipitate of barium carbonate, and sucrose was detected in the solution.

On the other hand, like the simple dialkyl carbonates, which undergo no measurable hydrolysis in 0·2N-acid at 35°,[9] the *O*-alkyloxycarbonyl derivatives of carbohydrates are more stable to acid than are many other carbohydrate esters and acetals.[10] Further, in the case of sucrose, the extreme acid-sensitivity of the glycoside link itself is considerably modified by even a low degree of substitution with *O*-alkyloxycarbonyl groups, presumably by steric inhibition.[11] A tri-*O*-ethoxycarbonylsucrose, being only slowly de-esterified

[9] Palomaa, Salmi, and Suoja, *Ber.*, 1939, **72**, 313.
[10] Ref. 7, p. 146.
[11] Shafizadeh, *Adv. Carbohydrate Chem.*, 1958, **13**, 24.

by acid, possesses higher glycosidic stability than sucrose octa-acetate (see Figure). The use of optical rotatory power to measure the extent of glycosidic hydrolysis is not completely valid in view of the possibility that the fructofuranose ⟶ fructopyranose conversion, which is mainly responsible for the large optical change (" inversion ") attending the hydrolysis of sucrose, may be blocked in some isomeric components by substitution at position 6'. However, the very slow development of reducing power during the acid hydrolysis of more highly substituted derivatives (average D.S. 5—8) supports the view that slight glycosidic fission rather than inhibited configurational change is responsible for the polarimetric observations. The *O*-methoxycarbonyl derivative prepared by Allpress and Haworth " displayed unexpected stability towards 1 per cent hydrochloric acid at 100° " and caused only slight reduction of Fehling's solution after 1 hour's boiling in 5% hydrochloric acid.[4] Octa-*O*-ethoxycarbonylsucrose was not immediately hydrolysed by concentrated sulphuric acid.

When a reaction mixture containing *O*-ethoxycarbonylsucroses for which only 5 mol. of reagents had been used was shaken with ether, not all the syrupy ester dissolved and three layers were obtained. The ether-insoluble derivative (average D.S. 3·3) polymerised at 150° *in vacuo*; it frothed vigorously and set rapidly to a horny mass, insoluble in all common organic solvents. The choice of this sample for a pyrolysis study was fortunate, since it later emerged that owing to its method of isolation it contained a trace of alkaline impurity which catalysed polymerisation and it was of such a degree of substitution as to possess a very short setting-time. These factors will be discussed in greater detail in Part II.[12]

## Experimental

Analyses are by the Scandinavian Microanalytical Laboratory, Copenhagen, and by University of Bristol analysts.

*General Method for the Preparation of* O-*Alkyloxycarbonylsucroses.*—The chloroformic ester (10 mol. per mol. of sucrose) and water (100 ml.) were stirred vigorously together, and any slight acidity of the aqueous phase was neutralised with solid sodium hydrogen carbonate. Sucrose (50 g.) was added and allowed to dissolve before the reaction flask was cooled to about −5°. Dropwise addition of 2N-sodium hydroxide (730 ml.) was then begun, the internal temperature being kept at 0° ± 2°. The syrupy derivatives were precipitated almost immediately, and after the alkali addition was complete (3 hr.) stirring was continued overnight, the mixture being left gradually to attain room temperature.

The esters were extracted with ether (2 × 500 ml.), except that for the *O*-methoxycarbonyl derivative chloroform was used, and the extracts were washed with water (2 × 500 ml.) and dried ($CaSO_4$). After being recovered by evaporation, the syrups were freed from traces of chloroformic esters by heating *in vacuo* at temperatures appropriate to the volatility of the reagent (*e.g.*, methyl, 80°/12 mm.; benzyl, 135°/5 × $10^{-4}$ mm.). The *O*-alkyloxycarbonylsucroses thus prepared were sparingly soluble in water or light petroleum, but dissolved readily in acetone, chloroform, and ethyl acetate. All except the *O*-benzyloxycarbonyl derivative were also soluble in methanol and ethanol, whilst all except the *O*-methoxycarbonyl esters dissolved in ether and benzene. The viscosity of the products decreased from the *O*-methoxycarbonylsucroses, a brittle glass at room temperature, to the *O*-butyloxycarbonyl esters, fairly mobile syrups. None reduced Fehling's solution.

*Paper Chromatography of* O-*Alkyloxycarbonylsucroses.*—Owing to their high mobility on untreated paper, the *O*-alkyloxycarbonylsucroses could not be separated by normal chromatographic techniques. Paper chromatography of the *O*-ethoxycarbonyl derivatives was carried out on Whatman No. 1 paper impregnated [6] with dimethyl sulphoxide, with a mobile phase of benzene–light petroleum (b. p. 60—80°; 4 : 1 v/v). Migration with light petroleum alone was negligible. After development for 3—4 hr. the papers were dried at 100° and sprayed with 2% w/v of potassium hydroxide in methanol, followed, after 5 min., by *p*-anisidine hydrochloride reagent [13] containing 5% v/v of concentrated hydrochloric acid. Careful heating revealed at least 5 components as brown spots. An *O*-methoxycarbonylsucrose (D.S. 6·8)

[12] Part II, following paper.
[13] Hough, Jones, and Wadman, *J.*, 1950, 1702.

provided only 3 spots by this technique, but showed at least 8 components when formamide was used as the stationary phase.[6] Separation of the *O*-ethoxycarbonyl derivatives was inferior when formamide or *NN*-dimethylformamide was used. The *O*-benzyloxycarbonyl ester (D.S. 8·0) appeared to be homogeneous. Owing to the difficulty of achieving reproducible impregnation of the paper with stationary phase, $R_F$ values are not recorded.

*The Reaction of Ethylene Dichloroformate with Sucrose.*—The dichloroformate [14] (27·4 g.), chloroform (100 ml.), and water (20 ml.) were stirred together vigorously and treated with a small amount of sodium hydrogen carbonate to neutralise slight acidity. Sucrose (10 g.) was added, and the chilled (ice–salt) stirred mixture treated dropwise during 2 hr. with 2N-aqueous sodium hydroxide (146 ml.), the temperature being kept at 0° ± 2°. A white flocculent polymer began to separate after 1 hr., increasing in amount during overnight stirring. Centrifugation of the thick suspension caused the polymer to accumulate between the chloroform and the aqueous phase. The liquids were decanted and the white product was freed from inorganic chloride by repeated centrifugation with water. Finally it was centrifuged twice with absolute ethanol, washed with ether, and collected by filtration. After drying *in vacuo* at 60°, the polymer (4·2 g., 31·2%) was insoluble in all common organic solvents including pyridine, *NN*-dimethylformamide and dimethyl sulphoxide. It shrunk slightly at about 270°, darkened, and decomposed without melting at 290—300°. Hydrolysis of the suspended polymer with 0·2N-barium hydroxide at room temperature, followed by neutralisation with carbon dioxide, filtration, and paper chromatography revealed sucrose as the sole carbohydrate constituent [Found: C, 41·6; H, 4·9; Ash, 0. $(C_{16}H_{24}O_{15})_n$ requires C, 42·1; H, 5·3%. $(C_{20}H_{27}O_{19})_n$ requires C, 42·1; H, 4·7%].

*Estimation of Total Hydrolysable Carbonate Group in O-Methoxycarbonylsucrose.*—An aliquot portion (10 ml.) of an approximately 2% w/v (accurately known) methanolic solution of vacuum-dried *O*-methoxycarbonylsucrose (OMe, 25·9%; D.S. 5·7) was transferred carefully to 0·125N-sodium hydroxide (50 ml.) in a covered beaker and heated for 5 min. on a boiling water-bath to complete the hydrolysis of ester groups. The solution was diluted with distilled water (50 ml.), gently stirred, and cooled to below 5°. It was then titrated slowly against 0·1N-sulphuric acid, with mixed Thymol Blue–Cresol Red as indicator [15] (4 drops), the tip of the burette being just covered by liquid. The end-point was taken as the first appearance of orange after the disappearance of blue, and the titration was repeated with a further aliquot part of the methanolic solution.

A blank titration was carried out similarly on the above sodium hydroxide solution (50 ml.), diluted with water (50 ml.) and methanol (10 ml.), and cooled to below 5°. Calculation of the inorganic carbonate formed by hydrolysis followed in the usual way [16] from the difference between the blank and the ester titres. The whole determination was repeated with fresh solutions of alkali and sucrose derivative (Found : $CO_2$, 37·45%; $CO_2$ : OMe, 1·44. Calc. for $CO_2Me$ group: $CO_2$ : OMe, 1·42).

*Octa-O-ethoxycarbonylsucrose.*—The partly esterified derivative (12·9 g.; D.S. 5·7), obtained by the aqueous alkali method, was dissolved in pyridine (50 ml.; KOH-dried) and the solution was cooled in ice–salt and treated cautiously (shaking) with ethyl chloroformate (32 ml.). Much fuming occurred but the temperature was easily kept below 0°. The mixture was then refrigerated, with occasional shaking, for 40 hr., then poured into water (2 l.), and the precipitated syrup was extracted with ether (1 l.). The extract was shaken repeatedly with N-hydrochloric acid until no further colour was removed, washed with water, dried ($CaSO_4$), decolorised with charcoal, and evaporated. The resulting syrup was further decolorised by shaking its solution in acetone with activated alumina. Final evaporation yielded 15·3 g. (97%) of very pale yellow syrup (Found: OEt, 38·8%; average D.S. 7·9). The product showed no OH absorption at 3530 cm.$^{-1}$, and crystallised, during several months, to colourless rosettes, m. p. 70—73°. Recrystallisation from ether–light petroleum (b. p. 40—60°) afforded *octa-O-ethoxycarbonylsucrose* in needles, m. p. 79—80°, $\nu_{max.}$ (C=O stretching) 1760 cm.$^{-1}$, $[\alpha]_D^{25}$ +43·8° (*c* 0·913 in EtOH) (Found: C, 47·0; H, 5·9; OEt, 39·9. $C_{36}H_{54}O_{27}$ requires C, 47·1; H, 5·9; OEt, 39·2%). In methanol solution at 20° the derivative gave an almost instantaneous precipitate with an excess of aqueous-methanolic barium hydroxide. Neutralisation of the

[14] Strain, U.S.P. 2,397,630 (*Chem. Abs.*, 1946, **40**, 3769).
[15] Simpson, *Ind. Eng. Chem.*, 1924, **16**, 709.
[16] Vogel, " A Textbook of Quantitative Inorganic Analysis," Longmans Green, London, 2nd edn., 1951, p. 242.

excess of alkali with carbon dioxide, followed by filtration and paper chromatography (butan-1-ol–pyridine–water, 10 : 3 : 3 v/v), indicated the presence of sucrose.

*Acid Hydrolysis of Sucrose Esters.*—The optical rotations of solutions of (*a*) sucrose (0·5% w/v in methanol), (*b*) sucrose octa-acetate (1% w/v in methanol), (*c*) *O*-ethoxycarbonylsucrose (D.S. 3·1; 9·05% w/v in ethanol) and (*d*) *O*-ethoxycarbonylsucrose (D.S. 4·9; 1·11% w/v in ethanol) were determined at 25°. Aliquot portions (9 ml.) were then mixed with concentrated hydrochloric acid (1 ml.), the solutions kept at 25°, and their optical rotations measured at intervals.

The hydrolysis of (*c*) was also followed chromatographically [Solvent: butan-1-ol–pyridine–water (10 : 3 : 3 v/v). Sprays: as above]. Components were attacked in the order of increasing $R_F$ value. Sucrose disappeared in 1—2 hr., esters with $R_F$ 0·34 (? mono-*O*-ethoxycarbonyl derivatives) in 24 hr. Ester(s) with $R_F$ 0·63 (? di-*O*-ethoxycarbonyl derivatives) were hydrolysed in 24 hr. to substances with $R_F$ 0·56 (pink with spray; ? mono-*O*-ethoxycarbonylglucoses) and $R_F$ 0·62 (yellow with spray; ? mono-*O*-ethoxycarbonylfructoses). No further change was then detected on paper chromatograms.

After 24 hr. the acid solutions of sucrose and its octa-acetate reduced Fehling's solution strongly. Treatment of solution (*b*) with barium hydroxide, followed by paper chromatography in the usual way showed that glycosidic hydrolysis was complete. Only very slight reduction of Fehling's solution was exhibited by (*c*) after 24 hr., and the more highly substituted ester (*d*) was non-reducing. All the esters in the Table were non-reducing after 3 hr. at 20° in 5N-aqueous-alcoholic hydrochloric acid and showed unchanged optical rotations after 48 hr. in N-acid.

Powdered octa-*O*-ethoxycarbonylsucrose (0·85 g.) was dissolved in concentrated sulphuric acid (10 ml.) at room temperature by stirring, and after 5 min. the colourless solution was poured into cold water (200 ml.). The resulting oily suspension was saturated with sodium chloride and extracted with chloroform (2 × 250 ml.), and the extract was washed with saturated sodium hydrogen carbonate and dried ($CaSO_4$). Evaporation gave 0·52 g. of pale yellow syrup (Found: OEt, 35·5%, equiv. to D.S. 6·2). Although the syrup strongly reduced Benedict's reagent, alkaline hydrolysis, followed by paper chromatography, showed sucrose esters to be present.

*Partial Solvent Fractionation of* O-*Ethoxycarbonylsucrose.*—Sucrose (50 g.) was caused to react with ethyl chloroformate (70 ml., 5 mol. per mol. of sucrose) and 2N-sodium hydroxide (365 ml., 5 mol.) at 0° ± 2° by the general method described above. A product began to separate early in the addition. After being stirred overnight, the total mixture was shaken vigorously with ether (500 ml.) and allowed to separate into three layers.

The syrupy lowest layer was run off and dried by repeated evaporation with benzene under reduced pressure, the final benzene solution being filtered. The clear colourless gum (40 g.) was dried at 60° *in vacuo* (Found: C, 46·1; H, 6·1; OEt, 25·3%, equiv. to D.S. 3·3; sulphated ash, 0·6%). The pH of 4% solution in 50% aqueous t-butyl alcohol was 8·2.

The ether layer was dried ($CaSO_4$) and concentrated (finally *in vacuo*) to 31 g. of colourless syrup (Found: OEt, 30·6%, equiv. to D.S. 4·6).

Paper chromatography of the aqueous layer (butan-1-ol–pyridine–water; 10 : 3 : 3 v/v) revealed traces of sucrose and some water-soluble esters, $R_F$ 0·34 and 0·63, which were not investigated.

*Polymerisation of* O-*Ethoxycarbonylsucrose.*—The ether-insoluble ester obtained by fractionation (D.S. 3·3; *ca.* 2 g.) was heated at 150°/12 mm. (oil-bath temperature). The initially mobile syrup bubbled vigorously, thickened, and set in 15 min. to a slightly discoloured horny mass with entrapped bubbles. Some further darkening occurred on prolonged heating (4 hr.). The powdered *polymer* was insoluble in water, alcohols, chloroform, acetone, and pyridine. It swelled but did not dissolve in dimethyl sulphoxide or *NN*-dimethylformamide (Found: C, 43·6; H, 5·7; OEt, 13·5%), $\nu_{max.}$ (C=O stretching) 1760 cm.$^{-1}$ (broad-based peak). On being heated, the polymer darkened slightly at 210° and decomposed without melting at 250—260°. Alkaline hydrolysis and paper chromatography indicated the presence of sucrose.

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# 1057. *Carbonic Esters of Sucrose. Part II.*[1] *The Polymerisation of O-Alkyloxycarbonylsucroses.*

By R. S. Theobald.

*O*-Ethoxycarbonylsucroses polymerise, with elimination of diethyl carbonate and ethanol, to form cross-linked resins when heated in the presence of an alkaline catalyst. The influence of the degree of substitution of the ester and its catalyst content upon polymerisation are discussed. A method for the direct preparation of an alkali-catalysed monomer from sucrose in high yield is described.

In Part I [1] the thermal polymerisation of a partially substituted *O*-ethoxycarbonylsucrose containing a trace of alkali was reported. Although the formation of condensation-polymers from aliphatic [2,3] and aromatic [3,4] carbonic esters is well known, and addition-polymers have been prepared from unsaturated *O*-alkyloxycarbonyl-carbohydrates [5-7] no other example of the thermal condensation of a carbohydrate carbonate to yield a cross-linked resin appears to have been published.

The polymerisation of *O*-ethoxycarbonylsucroses occurs most rapidly at temperatures above about 145°, and preferably under reduced pressure, which aids the removal of volatile by-products. The process is strongly catalysed by traces of alkali and inhibited by acids. To study the limitations imposed by the degree of substitution (D.S.) of the monomer, varying concentrations of sodium hydrogen carbonate were added to neutral ester samples (Table 1). With an increasing D.S., the setting-times produced by the same catalyst concentration were found to increase considerably. Likewise, the higher the D.S., the smaller the accelerating effect produced by a given rise in catalyst concentration.

Table 1.

Influence of degree of substitution and catalyst content upon the polymerisation of *O*-ethoxycarbonylsucroses.

| Average D.S. of monomer | Setting time (min. at 160° *in vacuo*) at varying concns. (% w/w) of $NaHCO_3$ | | | | Average OEt content of polymers |
|---|---|---|---|---|---|
| | 0·01 | 0·1 | 0·25 | 0·5 | (%) |
| 3·4 [a] | 40 | 4 | — | 3 | 14·8 |
| 4·7 [b] | 50 | 20 | 6 | 5 | 25·0 |
| 5·7 [c] | 90 | 60 | 45 | 25 | 27·3 |
| 7·9 [d] | N.S. | N.S. | N.S. | N.S. | — |

[a] Prepared from sucrose and 5 mol. of ethyl chloroformate, followed by ether-fractionation,[1] and removal of catalyst with air-dried cellulose powder (see Experimental). [b] Isolated from the ether extract of a 5 mol. preparation.[1] [c] Isolated from the ether extract of a 20 mol. preparation. [d] Prepared by further acylation of monomer, with D.S. 5·7, in pyridine.[1] N.S. = Not set in 6 hr.

As already indicated,[1] sufficient of an alkaline impurity to catalyse subsequent polymerisation may in certain circumstances accompany the *O*-ethoxycarbonylsucroses during their isolation from the preparation mixture. The solvent used for extraction has a profound effect upon the alkali content of the recovered esters (Table 2). Ether achieved a partial fractionation of the esters, but no catalyst passed into the ether phase. Benzene and chloroform each dissolved all of the syrup precipitated from a 5 mol. preparation, but differed greatly in their capacity to extract alkaline matter

[1] Part I, preceding paper.
[2] Carothers and Van Natta, *J. Amer. Chem. Soc.*, 1930, **52**, 314.
[3] Reynolds and Van Den Berghe, U.S.P. 2,789,509, 2,789,964—5, 2,789,967—8, 2,789,970; Reynolds and Dunham, U.S.P. 2,789,966, 2,789,969, 2,789,971—2/1957; Caldwell, U.S.P. 2,799,666/1957.
[4] Schnell, *Angew. Chem.*, 1956, **68**, 633; *Trans. J. Plastics Inst.*, 1960, **28**, 143.
[5] Muskat and Strain, U.S.P. 2,384,115/1945, 2,385,930/1945, 2,399,285/1946, 2,399,287/1946.
[6] Schwartz, Brown, and Tally, U.S. Dept. Agr., Bur. Agr. and Ind. Chem. Mimeo. Circ. Ser. 1952, AIC, 339, p. 9 (*Chem. Abs.*, 1953, **47**, 10,486).
[7] Zief, *J. Amer. Chem. Soc.*, 1950, **72**, 1137.

simultaneously. When benzene, the most effective of the three solvents, was used the proportion of alkali extracted decreased with increasing degree of substitution of the *O*-ethoxycarbonylsucroses, thus suggesting an association between the catalyst and the free hydroxyl groups of the esters. Furthermore, none of the sodium salts likely to be found in the reaction mixture was comparably soluble in benzene alone. Percival [8] has shown that sucrose itself readily forms addition compounds with potassium hydroxide, for example $C_{12}H_{22}O_{11},3KOH$, whilst in aqueous solution, particularly at low temperatures, acid carbonic esters of the type $C_{12}H_{21}O_{11}\cdot CO_2^-Na^+$ may exist.[9] The lower affinity of the higher *O*-ethoxycarbonylsucroses for alkali may account for the reduced influence of the total catalyst concentration upon setting time at higher D.S., already noted (Table 1).

Ethyl chloroformate is most economically employed in the preparation of sucrose esters of low D.S., and substitution at higher levels becomes increasingly less efficient (Table 2 and Part I [1]). The lowest D.S. at which an *O*-ethoxycarbonylsucrose becomes sufficiently hydrophobic to be isolated by solvent extraction appears to be 3. Such a trisubstituted ester possesses the additional advantage of a very short setting time *in vacuo* when suitably catalysed. The weights of the rapidly setting monomers obtained respectively from experiments B, D, and E (Table 2) represent yields of 74, 47, and 28% based on sucrose, and yields of only 55, 31, and 29% based on the chloroformic ester used. Incomplete separation of product from the saline phase, and only partial utilisation of sucrose, owing to the preferential formation of higher esters in the chloroformate phase, were believed to be responsible for these relatively low yields. By increasing the concentration of the

TABLE 2.

Influence of extraction solvent upon the alkali-content of *O*-ethoxycarbonylsucroses.

| Expt. | Reagents (mol.) per mol. of sucrose | Extraction solvent | Yield (g.) from 50 g. of sucrose | Average D.S. | % Alkali (calc. as $NaHCO_3$) | Setting time (min.) at 160° *in vacuo* |
|---|---|---|---|---|---|---|
| A | 10 | $C_6H_6$ | 100 | 4·8 | 0·0003 | 105 |
| B | 5 | $C_6H_6$ | 66 | 3·8 | 0·13 | 4 |
| C | 5 | $CHCl_3$ | 88 | 3·7 | 0·0009 | 40 |
| D | 5 | $Et_2O$ | 31 (extract) | 4·6 | Nil | Not set in 40 hr. |
| | | | 40 (insol.) | 3·3 | 0·24 | 4 |
| E | 3·3 | $C_6H_6$ | 24 | 3·5 | 0·23 | 4 |

aqueous alkali employed in the preparation, and by modifying the addition procedure to avoid its initial dilution, an optimum " salting-out " of triester, by the sodium chloride produced, was obtained. The tendency to polysubstitution in the ethyl chloroformate phase was minimised by adding an excess of light petroleum to the reaction mixture, to decrease the solubility of the trisubstituted ester in the reagent. By these means, alkali-catalysed *O*-ethoxycarbonylsucrose, with an average D.S. of about 3, was caused to be precipitated from the preparation mixture in 80% yield, based on ethyl chloroformate.

The polymerisation of " tri-*O*-ethoxycarbonylsucrose " at 160° *in vacuo* produced a liquid distillate which infrared analysis has shown to consist of almost equal proportions (w/w) of ethanol and diethyl carbonate. It seems likely that the polymerisation process itself is a simple alkali-catalysed transesterification (i), with the elimination of ethanol, and that the diethyl carbonate also isolated arises by simultaneous alkali-catalysed ethanolysis (ii) of some remaining *O*-ethoxycarbonyl groups. Examples of the direct elimination of diethyl carbonate between two *O*-ethoxycarbonyl groups to yield a carbonate polymer as in (iii) are known,[3] but such reactions appear to occur only at much higher temperatures (250°) and often only in the presence of a more specific catalyst, *e.g.*, tetrabutoxy titanium. On the other hand, *O*-ethoxycarbonyl groups have been shown to undergo alcoholysis very readily under certain conditions (see below). The polycarbonate from

[8] Percival, *J.*, 1935, 648.
[9] Smidt and Thamsen, *Acta Chem. Scand.*, 1956, **10**, 1172.

a trisubstituted *O*-ethoxycarbonylsucrose retains an average of about 1·5 *O*-ethoxycarbonyl groups per sucrose unit.

The availability of free hydroxyl groups for a type (i) reaction will decrease with the

$$XO{\cdot}CO_2Et + XOH \longrightarrow XO{\cdot}CO_2X + EtOH \quad \text{(i)}$$

(where X is a substituted sucrose radical)

$$XO{\cdot}CO_2Et + EtOH \longrightarrow XOH + Et_2CO_3 \quad \text{(ii)}$$

$$2XO{\cdot}CO_2Et \longrightarrow XO{\cdot}CO_2X + Et_2CO_3 \quad \text{(iii)}$$

extent of substitution in the monomer, until, in the case of octa-*O*-ethoxycarbonylsucrose no polymerisation occurs under normal conditions. It is also likely that in the more highly substituted esters (average D.S. 5—7) only those hydroxyl groups remain which, by virtue of steric hindrance or low acidity, are the least reactive. Such esters therefore show a much reduced affinity for an alkaline catalyst and velocity of polymerisation.

An approximately trisubstituted *O*-benzyloxycarbonylsucrose, obtained by solvent fractionation, has also been polymerised in the presence of alkaline catalyst. The process was more sluggish but was accompanied by less simultaneous alcoholysis than in the case of the corresponding *O*-ethoxycarbonyl ester. A distillate consisting chiefly of benzyl alcohol and dibenzyl carbonate in 4 : 1 ratio (w/w) was obtained.

Whilst the full evaluation of these polymers has not been completed, their susceptibility to alkaline hydrolysis (Table 3) is an obvious practical disadvantage. As expected, the problem is most serious with the less hydrophobic polymers from low-substituted esters, but variations apparently connected with the polymerisation conditions also occur. These variations are being studied. Hydrolysis of the polymers was progressive, even with a catalytic amount of alkali, presumably owing to the instability of sodium hydrogen carbonate in boiling solution.

TABLE 3.

Stability of polymerised *O*-ethoxycarbonylsucroses towards boiling alkaline soap solution.*

| D.S. of monomer | Setting time (min.) at 160° *in vacuo* | % Polymer recovered after boiling for ½ hr. | D.S. of monomer | Setting time (min.) at 160° *in vacuo* | % Polymer recovered after boiling for ½ hr. |
|---|---|---|---|---|---|
| 5·7 | 75 | 93 | 3·5 | 4 | 14 |
| 4·8 | 105 | 90 | 3·0 | 70 | 19 |
| 3·8 | 40 | 72 | 2·9 | 25 | 0 |
| 3·7 | 4 | 35 | | | |

* As used for the screening of potential textile finishing agents (Dr. J. Honeyman, personal communication).

The final cross-linking stage of the polymerisations may be carried out under pressure at about 160°. Hard, tough, moulded samples were produced from a mixture of partly polymerised " tri-*O*-ethoxycarbonylsucrose " with an equal weight of asbestos fibre as a " filler." Air-dried fillers based on cellulose inhibit the polymerisation to an extent probably related to their effective surface area (cellulose powder > cotton cloth > paper). This inhibiting effect, due to adsorption of the polymerisation catalyst on to the cellulose, may be prevented either by exhaustive drying of the filler or by its pre-treatment with very dilute aqueous sodium hydrogen carbonate.

The *O*-ethoxycarbonylsucroses undergo de-esterification by the lower primary, and to a smaller extent secondary, alcohols in the presence of an alkaline catalyst. t-Butyl alcohol is inactive. The reaction is reversible [10] but the equilibrium may be displaced to the right by the continuous crystallisation of sucrose. Thus, whilst catalysed *O*-ethoxy-

$$XO{\cdot}CO_2Et + ROH \underset{}{\overset{NaHCO_3}{\rightleftharpoons}} XOH + RO{\cdot}CO_2Et$$

[10] Theobald, Part III, following paper.

carbonylsucrose (D.S. 3·3) suffered complete alcoholysis in butan-1-ol alone during 6 hr. at 100°, the addition of dimethyl sulphoxide, to maintain homogeneous conditions, prevented any significant decomposition. Methanol, on the other hand, de-esterified the derivative even in the presence of the additional solvent.

## Experimental

*Polymerisations of* O-*Ethoxycarbonylsucroses Catalysed by Sodium Hydrogen Carbonate.*—The esters (*ca.* 5 g., accurately weighed) were dissolved in warm t-butyl alcohol (50 ml.) and treated with the requisite weight of sodium hydrogen carbonate in water (10 ml.), and the solutions evaporated *in vacuo*. Dehydration of the syrups was completed by two evaporations with benzene.

The polymerisations were carried out at 12 mm. in 50 ml. flasks heated in an oil-bath at 160°, and the time taken for all movement of the resinous mass just to cease was recorded as the "setting time" (reproducible to ±5% on samples of *ca.* 2—5 g.). Polymerisation was much slower below about 145° (a sample taking only 15 min. to set at 150° required 90 min. at 140°). Reduced pressure accelerated the polymerisation (15 min. at 12 mm. against 45 min. at 760 mm.).

*Solvent Extraction of* O-*Ethoxycarbonylsucrose Preparations.*—The preparations were conducted on a 50-g. scale by the general method described in Part I,[1] with 10, 5, or 3·3 mol. of the reagents per mol. of sucrose. Ether-fractionation of the 5-mol. preparation followed the procedure already given.[1] Benzene and chloroform extractions were carried out by decanting the saline phase from the precipitated esters, dissolving the latter in the solvent (500 ml.), and extracting the former with more solvent (2 × 250 ml.). The combined organic extracts were then immediately dried by azeotropic distillation at reduced pressure (fresh solvent being added if necessary), filtered, and finally evaporated to clear syrups.

*Estimation of Alkaline Catalyst in Esters.*—The syrups (3—5 g. approx., accurately weighed) were dissolved in warm ethanol (50 ml.) and diluted to 100 ml. with distilled water. The solutions were titrated potentiometrically against 0·01N-sulphuric acid, and the end-points determined graphically (*ca.* pH 5·5). The alkali-contents were calculated as % of sodium hydrogen carbonate (w/w).

*Modified Preparation of Approximately Trisubstituted* O-*Ethoxycarbonylsucrose.*—A vigorously stirred solution of ethyl chloroformate (46 ml, 3·3 mol.) in light petroleum (b. p. 100—120°; 250 ml.) was cooled in ice and treated dropwise with sucrose (50 g.) in 3N-sodium hydroxide (176 ml., 3·6 mol.). During the addition (4 hr.), the temperature was kept at 0—2°, and the level of the stirrer was adjusted to avoid serious dispersion of the precipitated esters. After overnight stirring, with the temperature rising slowly, the syrup was separated and dissolved in benzene (500 ml.), and the solution evaporated under reduced pressure at 60° to remove water. The process was repeated with further benzene until all turbidity had disappeared, and the final benzene solution was filtered and evaporated. This gave 69 g. (83·5% based on sucrose; 80% based on ethyl chloroformate) of a material with setting time 6 min. at 160° *in vacuo* (Found: OEt, 24·8%, equiv. to D.S. 3·1; sulphated ash, 1·1%, equiv. to Na 0·36%; free alkali by potentiometric titration, 0·06% w/w, calc. as $NaHCO_3$).

Separation of the heavy syrupy esters from the saline and the light petroleum phase was facilitated by fitting the reaction vessel with a wide-bore stopcock. A "constant-head" device contributed to regular alkali-addition.

*Examination of the Distillate from the Polymerisation of* O-*Ethoxycarbonylsucroses.*—The catalysed derivative (D.S. 3·25) from a modified preparation was dried for 4 hr. *in vacuo* at 60° and weighed (6·62 g.). The flask containing the dried syrup was connected to a weighed trap, the apparatus evacuated, and the trap immersed in acetone–carbon dioxide. Heating of the monomer was begun (oil-bath at 160°), and volatile products were rapidly condensed. After ½ hr. (setting time was 5 min.) heating was stopped and the distillate weighed (1·26 g.). Qualitative tests indicated the presence of diethyl carbonate and ethanol in the liquid. The infrared spectrum (700—4000 $cm.^{-1}$) was identical with that of an artificial 1 : 1 w/w mixture of diethyl carbonate and ethanol containing a trace of moisture.

*Preparation of Approximately Trisubstituted* O-*Benzyloxycarbonylsucrose.*—Sucrose (20 g.) was caused to react with benzyl chloroformate (40 g., 4 mol.) and 3N-sodium hydroxide (78 ml.,

4 mol.) at 0° by the general method of Part I.[1] After stirring overnight, the mixture was shaken with ether (200 ml.) to give three layers: ether (upper), syrup (middle, fraction A), and saline (lower).

The ether extract was further fractionated by addition of light petroleum (b. p. 60—80°; 20 ml.) to yield a syrup (fraction B) and a supernatant layer (fraction C). Chloroform-extraction of the saline layer removed only a negligible quantity of oil. The major fractions were dried ($CaSO_4$) (the syrups in chloroform solution), and the recovered *O*-benzyloxycarbonylsucroses heated at 120°/$10^{-4}$ mm. for 1 hr. to remove volatile impurities. Yields were: A (4·2 g.) (Found: C, 58·6; H, 5·8%; av. D.S.; 3·3); B (11·3 g.) (Found: C, 59·0; H, 5·6%; av. D.S., 3·4); C (11·5 g.) (Found: C, 62·2; H, 5·5%; av. D.S., 5·5).

*Polymerisation of* O-*Benzyloxycarbonylsucrose* (D.S. 3·3).—The derivative (A) (1·28 g.) was homogeneously mixed with sodium hydrogen carbonate (0·5% w/w) by the same procedure as for *O*-ethoxycarbonylsucroses. Polymerisation (at 165°/$10^{-2}$ mm.) and condensation of volatile products were carried out as before. The setting time (25 min.) was longer than that shown by a corresponding *O*-ethoxycarbonyl derivative. The distillate (0·22 g.) smelled of benzyl alcohol. Its infrared spectrum corresponded broadly to that of a 4 : 1 (w/w) mixture of benzyl alcohol and dibenzyl carbonate, but contained additional minor peaks at 1706 and 1725 cm.$^{-1}$.

The polymer (Found: C, 48·9; H, 5·0%) possessed similar solubility characteristics to those of polymerised *O*-ethoxycarbonylsucrose.

*Hydrolysis of Polymerised* O-*Ethoxycarbonylsucroses by Boiling Soap Solution.*—The polymers were finely ground and heated *in vacuo* at 160° for 50% of their previous setting times to complete cross-linking and to remove any volatile impurities, being afterwards reground if necessary. Samples (2 g.) were then heated for ½ hr. under reflux (stirring) with 50 ml. portions of a soap solution (0·5% w/v of " Sunlight " soap and 0·2% w/v of anhydrous sodium carbonate in water). The suspensions were diluted with water (50 ml.) and filtered whilst hot (suction), and the recovered polymers were washed with hot water (100 ml.) and dried to constant weight at 60° *in vacuo*. In one case (that from monomer with D.S. 4·8; Table 3), the recovered polymer was rehydrolysed, and the same percentage loss obtained, showing no significant change in the reactivity of the polymer after one hydrolysis treatment.

*Preparation of Asbestos-filled Discs from* O-*Ethoxycarbonylsucroses.*—An approximately tri-substituted derivative was polymerised at 160° *in vacuo* for 80% of its normal setting time (10 min.). The viscous resin was cooled, powdered, and distributed as evenly as possible throughout an equal weight of asbestos wool by kneading the mass with a small volume of chloroform. After being air-dried, the material was compressed (2 ton/sq. in.) in the centre of a steel washer separating two electrically heated (160°) platens. The hydraulic press was opened twice to add further solid and permit the escape of volatile products. Heating and pressure were continued for ½ hr.; a hard disc (sp. gr. *ca.* 1·4), unaffected by 24 hours' immersion in chloroform, was obtained.

On a large scale, the partial polymerisation of a rapidly setting derivative is preferably carried out at a somewhat lower temperature (*e.g.*, 140°), as the slower reaction allows more even heating of the sample.

*Use of Cellulose Fillers with* O-*Ethoxycarbonylsucroses.*—Catalysed " tri-*O*-ethoxycarbonylsucrose " (setting time 5 min. at 160° *in vacuo*), when shaken for a few minutes in chloroform solution with an equal weight of air-dried cellulose powder (" Ashless, for chromatography "), suffered complete loss of catalyst and did not polymerise in contact with the cellulose or when recovered (98%) as a syrup from the chloroform phase. Other forms of cellulose showed less severe prolongation of setting time, *e.g.*, cotton wool (55 min.), cotton cloth (20 min.), and filter-paper (6 min.).

Cellulose powder, dried *in vacuo* at room temperature over phosphoric oxide or at 160°, had no inhibiting effect on polymerisation. Cellulose powder, stirred with 1% w/v aqueous sodium hydrogen carbonate, collected, and air-dried, could also be used in the preparation of discs.

*Alcoholysis of* O-*Ethoxycarbonylsucroses.*—Samples (1—2 g.) of " catalysed " *O*-ethoxycarbonylsucrose (D.S. 3·3) obtained from a modified preparation, were heated with various alcohols (10—20 parts by vol.) on the steam-bath under reflux for 6 hr. The solutions were then examined chromatographically (Part I [1]), with the initial ester as reference material.

De-esterification to sucrose was complete in methanol, ethanol, and butanol, but only partial in propanol. Crystallisation of the sucrose was particularly rapid from butanol. Repetition of the experiments in the presence of dimethyl sulphoxide (10 parts) caused complete alcoholysis

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only in the case of methanol. Attack was partial with ethanol, less with propanol, and negligible with butanol.

In the absence of additional solvent, propan-2-ol and butan-2-ol caused only partial de-esterification of the same derivative in 6 hr. A new substance, $R_F$ 0·43 (butan-1-ol–pyridine–water 10 : 3 : 3 v/v), was detected in the former case but was not isolated. t-Butyl alcohol was without effect. Alkali-free ester samples were not de-esterified by methanol.

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## 1058. *Carbonic Esters of Sucrose. Part III.*[1] *The Direct Preparation of Poly(sucrose Carbonates) from Sucrose.*

By R. S. THEOBALD.

Sucrose reacts with carbonyl chloride in the presence of pyridine to form poly(sucrose carbonate). Both soluble and insoluble polymers are more conveniently prepared by the action of diphenyl carbonate on sucrose in the presence of an alkaline catalyst. Soluble poly(sucrose carbonate) is almost inert towards invertase and shows a much higher stability to acid than sucrose does. The possible relevance of these properties and of some periodate oxidation studies to the structure of the polymer is discussed.

THE formation of a carbonate polymer from sucrose and ethylene dichloroformate in the presence of aqueous alkali has been reported.[2] Carbonyl chloride provides an even simpler example of a difunctional reagent capable of forming intermolecular carbonate bridges, and has been employed for this purpose in both one-stage and two-stage condensation reactions with polyhydric alcohols[3] or phenols.[4,5] In their preparations of the monosaccharide carbonates by reaction of carbonyl chloride with the sugars in pyridine, Haworth and Porter[6] obtained amorphous by-products which, although not characterised, were probably polymeric.

The structural inability of sucrose to accommodate a five-membered cyclic carbonate group,[2] and, on the other hand, its high capacity for substitution, might be expected to favour the formation of a cross-linked polycarbonate with carbonyl chloride. Attempts to use aqueous alkali, under a variety of conditions, as the acid-acceptor in such a reaction were largely unsuccessful, the maximum yield of polymer achieved being about 4%. Whilst sodium hydroxide is an effective condensing agent in the preparation of aromatic polycarbonate resins,[5] its use with strongly hydrophilic derivatives such as carbohydrates appears to be limited by the rapid hydrolysis of the polycarbonate. In pyridine solution a polycarbonate was more easily obtained from sucrose, but the reaction tended to be uncontrollable and high molar ratios of carbonyl chloride to sucrose were required for satisfactory conversion.

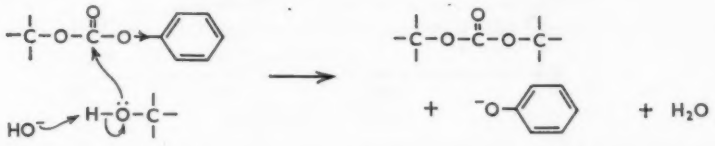
The amorphous nature of the " carbonate " synthesised in 1912 by Hochstetter[7] from sucrose and diphenyl carbonate at 130° possibly indicated a polymeric structure, and it prompted a re-investigation of this largely neglected type of transesterification. Use of the recommended solvent, namely, molten resorcinol, gave no product with the characterstics claimed by Hochstetter, that is, a sparing solubility in water and alcohols. The

[1] Part II, preceding paper.
[2] Part I, Theobald, *J.*, 1961, 5359.
[3] Muskat and Strain, U.S.P. 2,384,115, 2,385,930, 2,399,285, 2,399,287.
[4] Einhorn, *Annalen*, 1898, **300**, 135.
[5] Schnell, *Angew. Chem.*, 1956, **68**, 633; *Trans. J. Plastics Inst.*, 1960, **28**, 143.
[6] Haworth and Porter, *J.*, 1930, 151.
[7] Hochstetter, G.P. 268,452/1912; *Friedländer*, 1913, **11**, 1211.

predominant reaction, even with very pure reagents, was hydrolysis of the sucrose. However, addition of a catalytic amount of sodium hydrogen carbonate caused rapid gelling of the mixture, and an amorphous substance with the correct physical properties resulted. This proved to be a cross-linked poly(sucrose carbonate) containing probably some *O*-phenoxycarbonyl groups and possibly resorcinol in a similar state of combination.

The apparent necessity for an alkaline catalyst contrasts with Hochstetter's conclusion [7] that superior yields result from the omission of catalyst, and it seems not to be attributable to possible differences in the apparatus used. Soda glass was shown chromatographically to catalyse polymerisation very slightly and to decrease " inversion " of the sucrose, but its effect was undoubtedly masked by the feebly acid character of resorcinol ($k_1 = 3{\cdot}6 \times 10^{-10}$ at 18°). In the neutral solvent dimethyl sulphoxide, however, soda glass exerted a powerful catalytic action and rapid gelling occurred, with no hydrolysis of the sucrose. A sodium hydrogen carbonate catalyst (0·1% w/w) in dimethyl sulphoxide caused conveniently swift polymerisation even at 100°.

Under the last conditions, replacement of diphenyl carbonate, as the carbonate source, by the diethyl ester led mainly to the formation of *O*-ethoxycarbonylsucroses of low degrees of substitution, with negligible polymerisation. This difference in behaviour may reflect the higher electrophilic activity of the *O*-phenoxycarbonyl groups,[8] which participate spontaneously in intermolecular condensation until a semi-rigid structure is attained. Similar attempts to utilise ethylene carbonate for the production of cross-linked carbonate polymers were unsuccessful, the main reaction in this case probably being polyether formation.[9]



The effect of reducing the proportion of diphenyl carbonate relative to sucrose, from the 4 : 1 molar ratio employed by Hochstetter to a 0·5 : 1 ratio, is summarised in the Table.

Composition of polycarbonates obtained from sucrose and diphenyl carbonate in catalysed dimethyl sulphoxide.

| Mol. of $Ph_2CO_3$ per mol. of sucrose | Gelling time (min.) at 135° | Yield of polymer (g.) from 14 g. of sucrose | Found (%) C | H | Phenol | *O*-Phenoxycarbonyl groups per sucrose unit (calc. from % phenol) |
|---|---|---|---|---|---|---|
| 0·5 | No gelling in 1 hr. | 13·7 (sol.) | Not analysed | | | — |
| 0·9 | No gelling in 1 hr. | 13·1 ,, | ,, | ,, | | — |
| 1·0 | 6 | 11·3 (sol.) | 42·1 [c] | 5·4 [c] | — | — |
| | | 4·9 (insol.) | Not analysed | | | — |
| 1·1 | 8 [a] | 8·65 ,, | 42·9 | 5·7 | 0·09 | 0·004 |
| 1·3 | 4 | 13·1 ,, | 42·7 | 5·5 | 0·21 | 0·01 |
| 1·5 | 4 | 14·9 ,, | 42·7 | 5·4 | 0·46 | 0·02 |
| 2·0 | 7 [a] | 16·8 ,, | 43·9 | 5·1 | 3·4 | 0·14 |
| 4·0 | 4 [b] | 17·7 ,, | 47·5 | 4·7 | 13·5 [d] | 0·65 |

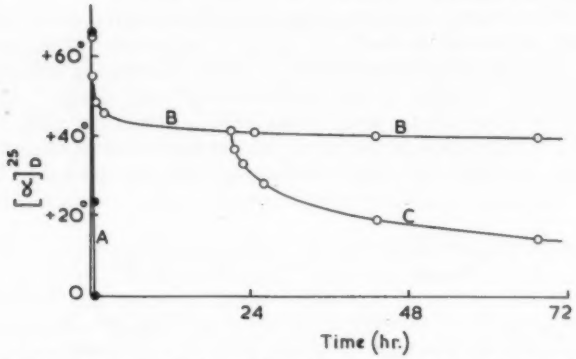
[a] At 130°. [b] 17 min. at 100°. [c] After dialysis. [d] 13·3% in polymer from reaction heated 4 hr.

At the higher level the polymer contained an average of about 0·7 *O*-phenoxycarbonyl group per sucrose residue, irrespective of the duration of heating after gelling. The *O*-phenoxycarbonyl content fell significantly as the amount of reagent was reduced, until

[8] Hammett, " Physical Organic Chemistry," McGraw-Hill Book Co., New York, 1940, p. 211.
[9] Monson and Dickson, U.S.P. 2,819,260/1958 (*Chem. Abs.*, 1958, **52**, 10,166).

with about 1·5 mol. an almost theoretical yield of cross-linked polymer, with negligible *O*-phenoxycarbonyl substitution, was obtained. Equimolar proportions of sucrose and diphenyl carbonate afforded a poly(sucrose carbonate) 70% of which was water-soluble, and a further decrease in the reagent (*e.g.*, to 0·9 mol. per mol. of sucrose) gave a wholly water-soluble polymer which could be purified by dialysis.

A dialysed water-soluble poly(sucrose carbonate), when incubated with invertase, exhibited a small rapid fall in optical rotation and was then attacked only extremely slowly by the enzyme. Although very little is known concerning the specificity of invertase towards substituted sucroses, it seems likely that a derivative substituted solely in the D-glucopyranose half of the molecule would undergo enzymic hydrolysis. Thus, sucrose 2-phosphate [10] is attacked, as also are methyl [11] and benzyl β-D-fructofuranoside.[12] Most of the fructose residues in the polymer therefore probably carry carbonate linkages, and the initial enzyme attack is possibly confined to chain-terminating sucrose units. Only




Hydrolysis of poly(sucrose carbonate) by invertase and by N-hydrochloric acid.

(A) Upper section(s) of hydrolysis curves of sucrose in either aqueous invertase or N-hydrochloric acid (curves coincident in this range). (B) Undialysed poly(sucrose carbonate) in aqueous invertase. (C) Undialysed poly(sucrose carbonate) in aqueous invertase treated, after 21 hr., with hydrochloric acid (Calc. for complete hydrolysis: $[\alpha]_D$ −37·2°).

fructose, and not glucose, is liberated in this step, but it may not be valid to conclude that substitution in D-fructofuranose is restricted to positions sterically shielding the glycoside bond. Mineral acids caused progressive hydrolysis of soluble poly(sucrose carbonate), but much more slowly than in the case of sucrose itself (see Figure). A positive optical rotation was still obtained after 1 week at 25° in N-acid, behaviour analogous to that already reported [2] for " tri-*O*-ethoxycarbonylsucrose."

Oxidation of the dialysed polymer with sodium metaperiodate, followed by reduction with potassium borohydride, and hydrolysis with a cation-exchange resin provided much free glucose, indicating [13] appreciable substitution at $C_{(3)}$ of the D-glucopyranosyl residue. However, the total periodate consumption of about 2 mol. per sucrose unit (48 hr.) requires that an equal proportion of polymer linkages must occupy primary positions (6, 1′, or 6′). Further examination of the hydrolysis fragments also revealed fructose and a trace of erythritol, consistent with some secondary substitution, at positions 3′ or 4′, in the D-fructofuranosyl moiety, and at $C_{(4)}$ of D-glucopyranose. The failure to detect glyceraldehyde, a

[10] Courtois and Ramet, *Bull. Soc. Chim. biol.*, 1945, **27**, 610, 614.
[11] Hestrin and Avineri-Shapiro, *Biochem. J.*, 1944, **38**, 2; Purves and Hudson, *J. Amer. Chem. Soc.*, 1934, **56**, 1973.
[12] Purves and Hudson, *J. Amer. Chem. Soc.*, 1937, **59**, 49.
[13] Smith and Van Cleve, *J. Amer. Chem. Soc.*, 1955, **77**, 3091.

fragment indicative of 2-substitution in glucose, should not be regarded as conclusive, since the chromatographic standard of this compound was itself only weakly revealed.

A similar structural study commencing with periodate oxidation was carried out on "tri-*O*-ethoxycarbonylsucrose." For this and other related oxidations, 20% t-butyl alcohol in water was found to be a suitably inert solvent, though exerting the same inhibiting effect at higher concentrations as noted by Guthrie [14] for *NN*-dimethylformamide. The ester consumed only about 1 mol. of oxidant per mol. of sucrose in 5 days, but paper chromatograms of the fragments from subsequent reduction and hydrolysis were indistinguishable from those obtained from soluble poly(sucrose carbonate). These results, in conjunction with the observed acid-stability of the derivatives, suggest that in both poly(sucrose carbonate) and *O*-ethoxycarbonylsucrose substitution is partly random, but mainly preferential at positions 3, 6, 1′, and 3′. The strong possibility of acyl migration under slightly alkaline conditions [15] renders any structural investigation involving standard methylation techniques of little value.

In very few cases have the detailed structures of partly substituted sucrose derivatives been determined. Black, Dewar, and Rutherford [16] concluded that in a mono-*O*-methylsucrose, obtained from trisodium "sucrate," the ether groups occupy mainly, but not exclusively, positions 2, 6, 1′, and 3′. According to Gaver *et al.*,[17] a preference for initial attack at $C_{(2)}$ is also exhibited by sucrose in sodium hydroxide–butanol, further substitution involving, successively, positions 3′ and 3. However, Percival [18] claimed that potassium hydroxide forms an adduct ($C_{12}H_{22}O_{11}$,3KOH) with sucrose exclusively at the primary positions (6,1′,6′). The difficulty of avoiding the selective isolation or detection of particular isomers in these researches may partly explain apparent inconsistencies. It also seems likely that, with larger attacking groups, steric factors may take precedence over hydroxyl acidities in deciding the positions of substitution.

## Experimental

The following chromatographic solvents were employed with Whatman No. 1 paper: (i) butan-1-ol–pyridine–water (10 : 3 : 3 v/v), (ii) butan-1-ol–pyridine–water (3 : 2 : 1·5 v/v), (iii) butan-1-ol–ethanol–water (40 : 11 : 19 v/v), and (iv) ethyl acetate–acetic acid–water (9 : 2 : 2 v/v). Sprays used for detection were (*a*) methanolic potassium hydroxide–acidified *p*-anisidine reagent,[3] (*b*) 0·02M-sodium metaperiodate followed after 5 min. by 4% ammoniacal silver nitrate,[19] and (*c*) *p*-anisidine hydrochloride.[20]

*Reaction of Sucrose with Carbonyl Chloride in Pyridine.*—Carbonyl chloride (43·7 g., 5 mol.) in dry toluene (100 ml.) was added dropwise during 1 hr. to a cooled (ice–salt) stirred solution of sucrose (30·2 g.) in dry pyridine (500 ml.). The mixture was stirred for a further ½ hr. at room temperature, then poured into saturated aqueous sodium hydrogen carbonate (2 l.), and the precipitate was collected. After being washed thoroughly with water it was dried *in vacuo* over phosphoric oxide. The yield of cross-linked *poly(sucrose carbonate)* was 8·7 g. (26%) (Found: C, 42·4; H, 5·2. $[C_{12}H_{20}O_{11},CO]_n$ requires C, 42·4; H, 5·4; $[C_{12}H_{19}O_{11}\cdot(CO)_2]_n$ requires C, 42·5; H, 4·8%), $\nu_{max.}$ (C=O stretching) 1760 cm.$^{-1}$. A similar experiment with stirring overnight after addition of the reagent afforded a 28% yield of polymer, but recovery was negligible when only 2 mol. of carbonyl chloride was used per mol. of sucrose. An unknown excess of gaseous carbonyl chloride, passed into sucrose in pyridine, gave on one occasion a 50% yield of polymer.

The polymer was rapidly hydrolysed by an excess of aqueous ammonia at room temperature and sucrose was detected chromatographically in the solution.

*Reaction of Sucrose with 4 Mol. of Diphenyl Carbonate.*—(a) *In resorcinol.* Hochstetter's

[14] Guthrie, *Chem. and Ind.*, 1960, 691.
[15] McKeown and Hayward, *Canad. J. Chem.*, 1957, **35**, 992.
[16] Black, Dewar, and Rutherford, *J.*, 1959, 3073.
[17] Gaver, Lasure, and Tieszen, U.S.P. 2,572,923 (*Chem. Abs.*, 1952, **46**, 1786).
[18] Percival, *J.*, 1935, 648.
[19] Dr. A. C. Richardson, personal communication.
[20] Hough, Jones, and Wadman, *J.*, 1950, 1702.

method [7] was modified as follows: Sucrose (7 g.) was dissolved in a magnetically-stirred mixture of molten resorcinol (35 g.) and sodium hydrogen carbonate (0·035 g.) at 135° (oil-bath). Diphenyl carbonate (18 g.) was added and heating continued for about 45 min.; sudden cessation of stirring then denoted gelling of the mixture. The cooled mass was macerated with ether (500 ml.), and the polymer was collected, washed with more ether, and air-dried. After being triturated with water and collected, it was continuously extracted (Soxhlet) over boiling aqueous dioxan (1 : 1 v/v) for 8 hr., and vacuum-dried (60°; silica gel). The poly(sucrose carbonate) (5·4 g.) was insoluble in ethanol and other common organic solvents, but rapidly dissolved in cold aqueous alkalis with hydrolysis to sucrose. Continuous ether-extraction of the acidified (dilute sulphuric acid) hydrolysate afforded a small quantity of dark oil containing resorcinol (fluorescein test) and probably phenol. Analysis of the polymer also supported the presence of some aromatic residues (Found: C, 44·0; H, 4·8%).

With 1% of catalyst (w/w of resorcinol) gelling occurred in about 10 min. With the omission of catalyst and the use of purified reagents ("AnalaR" sucrose; resorcinol recrystallised three times from ethanol–benzene; diphenyl carbonate recrystallised three times from ethanol) in a Pyrex flask no gelling took place in 4 hr. at 135°. Addition of ether precipitated a pinkish solid (101% w/w of sucrose used) consisting almost exclusively of sucrose and its hydrolysis products, as indicated by paper chromatography. A duplicate experiment did not give a gel in 20 hr. at 130°, and the residue remaining from subsequent distillation at 150°/$10^{-4}$ mm. was totally ethanol-soluble.

(b) *In dimethyl sulphoxide, catalysed by soda glass.* Sucrose (14 g.) in warm dimethyl sulphoxide (20 ml.; redistilled from $K_2CO_3$) was treated with recrystallised diphenyl carbonate (36 g.). The stirred solution was kept at 135° and powdered soda glass (1 g.) added. Gelling occurred suddenly after 5 min. The use of coarsely ground soda glass (1 g.) as the catalyst prolonged the gelling time to 30 min. Pyrex glass (1 g.) caused no gelling in 2 hr., and paper chromatography of the brown syrup precipitated by ether indicated almost complete decomposition to glucose, fructose, and 5-hydroxymethylfurfuraldehyde.

*Alkaline Hydrolysis of Cross-linked Poly(sucrose Carbonate).*—Polycarbonate gels, prepared by method (b) above but with sodium hydrogen carbonate (0·02 g.) as the catalyst, with varying molar ratios of diphenyl carbonate to sucrose (see Table), were purified and dried as in (a) [$\nu_{max.}$ (C=O) 1760 cm.$^{-1}$ for all samples].

The polymers (*ca.* 2 g., accurately weighed) were hydrolysed at 60° with 2N-sodium hydroxide (100 ml.) for 30 min., and the clear solutions carefully acidified with dilute sulphuric acid. Bromine water was added slowly (shaking) until a faint yellow colour persisted in the aqueous phase. The precipitated 2,4,6-tribromophenol (m. p. 91—93°; mixed m. p 93—95°) was collected (suction), washed with water (50 ml.), and dried at room temperature and pressure over phosphoric oxide. The average number of *O*-phenoxycarbonyl groups per sucrose unit of polymer was calculated from the yield of tribromo-derivative obtained. No correction was made for the slight solubility of tribromophenol ($7 \times 10^{-3}$% in water at 15°, equivalent to *ca.* 0·008 *O*-phenoxycarbonyl group per 200 ml. of hydrolysate).

Re-extraction of the polymers with aqueous dioxan for a further 8 hr. caused no decrease in the phenol obtained by hydrolysis.

*Reaction of Sucrose with 1 Mol. of Diphenyl Carbonate.*—Sucrose (14·0 g.; dried over $H_2SO_4$) and diphenyl carbonate (8·76 g., 1 mol.; recryst.) were heated together at 135° in dimethyl sulphoxide (20 ml.) containing sodium hydrogen carbonate (0·02 g.) in the usual way. The solution gradually became more viscous, finally appearing to gel in 6 min. After a further 5 min., the mixture was cooled and transferred to acetone (250 ml.), and the precipitated product collected when granular, triturated with acetone and ether, and dried *in vacuo* (over $H_2SO_4$) (yield 18·4 g.).

The gelatinous suspension obtained by stirring the solid with water (200 ml.) was centrifuged (2000 rev./min.), giving 4·86 g. of insoluble polycarbonate (A). De-ionisation of the supernatant solution by electrodialysis [21] (B.D.H. "Permaplex" membranes A-20 and C-20; ~250 v) and evaporation *in vacuo* afforded 11·13 g. of crude water-soluble polymers (B). Multiple development paper chromatography [22] of the soluble fraction [four overnight developments with solvent (ii), the paper being dried after each run; spray (*a*)] separated sucrose and at least five other components from the virtually non-mobile high-polymer spot.

[21] Anderson and Wylam, *Chem. and Ind.*, 1956, 191.
[22] Jeanes, Wise, and Dimler, *Analyt. Chem.*, 1951, **23**, 415.

Dialysis (Cellophane membrane) of the water-soluble fraction removed low polymers and a trace of sucrose, leaving soluble *poly(sucrose carbonate)* (C), recovered as a brittle resin, insoluble in non-polar solvents, but soluble in water, *NN*-dimethylformamide, and dimethyl sulphoxide, with $[\alpha]_D^{25}$ +70·3° (*c* 2·2 in $H_2O$), $\nu_{max.}$ (C=O) 1750 cm.$^{-1}$ (Found: C, 42·1; H, 5·4. $[C_{13}H_{20}O_{12}]_n$ requires C, 42·4; H, 5·4%).

*Action of Invertase on Soluble Poly(sucrose carbonate).*—(a) *Polarimetric study.* A solution of the de-ionised, but undialysed, polymer B (2 g.) in water (40 ml.) was treated with B.D.H. invertase concentrate (0·5 ml.), quickly diluted to 50 ml., and kept at 25°. The optical rotation was measured at intervals (see Figure).

A solution of the dialysed polymer C (0·219 g.) and invertase concentrate (0·1 ml.) in water (10 ml.) was similarly examined. The fall in rotation in 24 hr. ($[\alpha]_D^{25}$ +70·3° ⟶ +64·0°) was equivalent to the hydrolysis of about 7% of the total sucrose content of the polymer.

(b) *Examination of products.* Dialysed polymer C (0·4 g.) in water (2 ml.) was treated with invertase concentrate (0·1 ml.) and kept 24 hr. at room temperature. This solution, and that from a simultaneous hydrolysis of sucrose (0·02 g.), were examined on paper chromatograms [solvents (i) and (iv); sprays (*a*) and (*b*)]. Fructose, but not glucose, was detected in the polymer hydrolysate whereas both were easily detected in the sucrose hydrolysate.

Subsequent dialysis of the polymer hydrolysate removed fructose, as shown by paper chromatography, leaving a polymer solution that was weakly reducing towards Fehling's reagent. The initial polymer C was non-reducing.

*Acid Hydrolysis of Soluble Poly(sucrose carbonate).*—The invertase hydrolysate (9 ml.) of polymer B, after 21 hr. at 25°, was mixed with concentrated hydrochloric acid (1 ml.) and kept at 25°. The optical rotation was measured at intervals and plotted (see Figure).

*Periodate Oxidation of Dialysed Polymer.*—Dialysed, dried poly(sucrose carbonate) (0·2046 g.) in water (20 ml.) was treated with 0·1M-sodium metaperiodate (15 ml.), and the solution diluted to 50 ml. with water and kept in the dark at room temperature. After 48 hr. an aliquot part (5 ml.) was removed and the periodate uptake estimated by the potassium iodide–thiosulphate method [23] (Found: 1·97 mol. per sucrose unit). After 3 days, excess of saturated aqueous barium chloride was added to the bulk of the oxidation medium, the mixture made faintly alkaline with saturated aqueous barium hydroxide, and then neutrality was restored with carbon dioxide. The inorganic precipitate was collected, the filtrate evaporated *in vacuo* below 40°, and the residue treated with ethanol (50 ml.). After a further evaporation to remove traces of water, the white solid was extracted at room temperature with absolute ethanol (4 × 50 ml.), and the extracts were filtered and evaporated below 40° to an almost clear syrup (0·23 g.). This was dissolved in water (10 ml.), and treated, in ½ hr., with potassium borohydride (0·5 g.). The solution, after being kept overnight, was diluted to 50 ml. with water and slowly percolated through a column (35 × 2 cm.) of Amberlite IR-120 ($H^+$) resin. The eluate and column washings (200 ml.) were together evaporated *in vacuo* below 40° to about 10 ml., treated with methanol (50 ml.), and taken almost to dryness. After three further evaporations with methanol, to remove boric acid, a syrup (0·15 g.) remained.

Paper chromatography of the syrup was carried out with dihydroxyacetone, glycerol, erythritol, glyceraldehyde, glycolaldehyde, sucrose, glucose, and fructose as reference compounds, with solvents (i), (iii), and (iv), and sprays (*b*) and (*c*). The following components were detected: glucose (strong), glycerol (strong), dihydroxyacetone (fairly strong), fructose (fairly strong), and erythritol (trace). Whilst glycollaldehyde and glyceraldehyde were not detected, the corresponding standards were only weakly revealed.

*Periodate Oxidation of "Tri-O-ethoxycarbonylsucrose."*—The dried derivative (D.S. 3·2; 0·210 g.) was dissolved in warm t-butyl alcohol (10 ml.), cooled, and treated with 0·1M-sodium metaperiodate (15 ml.), followed by water to a volume of 50 ml. The solution was kept in the dark at room temperature for 5 days (uptake 1·08 mol. per mol. of sucrose), then worked up as above except that (i) the residue of barium salts was washed with 50% aqueous t-butyl alcohol in place of water, (ii) borohydride reduction was conducted in 50% aqueous ethanol, and (iii) the resin column was washed before and after use with 50% ethanol. The final syrup (0·104 g.) was chromatographed exactly as before. The same hydrolysis fragments were detected as for the polycarbonate, in approximately the same proportions.

Sucrose itself consumed 2·97 mol. of periodate in 5 days in 20% t-butyl alcohol.

*Action of Diethyl Carbonate on Sucrose.*—Sucrose (7 g., 1 mol.), diethyl carbonate (10·2 ml.,

[23] Neumüller and Vasseur, *Arkiv Kemi*, 1953, **5**, 235.

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4 mol.), and sodium hydrogen carbonate (0·02 g.) in dimethyl sulphoxide (20 ml.) were stirred under reflux at 130° for 2 hr. The solution was cooled and poured into an excess of ether, and a sample of the syrupy precipitate chromatographed on paper [solvent (iii); spray (*a*)]. Much unchanged sucrose was detected, but strong spots ($R_F$ 0·41 and 0·66) corresponding to the low-substituted esters found previously [2] in " tri-*O*-ethoxycarbonylsucrose " were also revealed. Slow-moving polymeric components were present in traces only.

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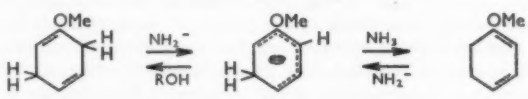
## 1059. *The Base-catalysed Isomerisation of Some 3-Alkyldihydroanisoles.*

By A. J. BIRCH, (MRS.) E. M. A. SHOUKRY, and F. STANSFIELD.

Isomerisation with sodamide in liquid ammonia of the 3-alkyldihydroanisoles (IV) containing unconjugated double bonds gives the exocyclic conjugated dienes (VI) as the final product if R′ = R″ = H or R′ = H, R″ = Me, but the endocyclic isomer (V) is obtained if R′ = R″ = Me. Reduction by sodium and propan-2-ol in liquid ammonia of 3,4-dimethylanisole (VII) and of 6-methoxy-1,2,3,4-tetrahydronaphthalene (IX), followed by similar isomerisation, gives the endocyclic dienes (VIII) and (X). The mechanisms involved are discussed.

REDUCTION of alkylanisoles with sodium and ethanol in liquid ammonia gives chiefly dihydroanisoles containing unconjugated double bonds as the result of kinetically controlled reactions.[1,2,3] In the presence of an alkali-metal amide in liquid ammonia, these dienes are converted into the more stable conjugated isomers, usually by turning of a double bond about the carbon atom bearing the methoxyl group. This has been shown [3,4] to be due to establishment of an equilibrium of the type shown below. Apart from their intrinsic interest, a study of such reactions is important in understanding the course of reductions by lithium and various amines, since such equilibrations are clearly involved and permit reduction to occur past the dihydro-stage.[2]




Because 2,5-dihydroanisole is converted into 2,3-dihydroanisole as above, it was expected that 2,5-dihydro-3-methylanisole (I) would give the homologue (II). In fact this is produced to some extent, as shown by the diene reaction with dimethyl acetylenedicarboxylate.[5] However, it was noted [6] that if the isomerisation proceeded for a long time, and in particular if the ammonia evaporated, a different product was obtained. This has now been shown to be the exocyclic diene (III) and it has been found that the endocyclic diene (II) cannot be prepared by this method in a state of purity because its rate of isomerisation to the diene (III) is comparable with its rate of formation.

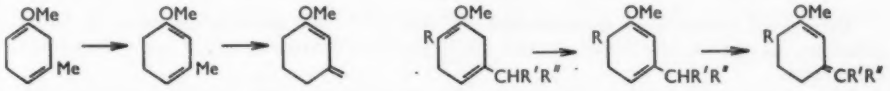
The courses of these and analogous reactions were followed by means of ultraviolet spectra. The unreduced alkylanisoles have twin peaks,[7] $\lambda_{max.}$ 270—279 and 277—288 mμ,

[1] Birch, *J.*, 1944, 430.
[2] Birch, *J.*, 1946, 593.
[3] Birch, *J.*, 1950, 1551.
[4] Birch, *J.*, 1947, 1642.
[5] Birch and Hextall, *Austral. J. Chem.*, 1955, **8**, 96.
[6] Birch, unpublished work.
[7] Burawoy and Chamberlain, *J.*, 1952, 2311.

whereas endocyclic and exocyclic dienes have single peaks, $\lambda_{max.}$ 267—270 and 244—250 mμ, respectively. Unconjugated dienes show only end absorption in the region 200—220 mμ. Similar differences between endo- and exo-cyclic dienes exist also in the steroid [8] and terpene [9] series, but the values observed here for the exocyclic (*trans*) dienes are higher than the calculated values [10] (*ca.* 230 mμ) probably owing to an extension of conjugation to the methoxyl group. In contrast, the endocyclic (*cis*) dienes show little evidence of such an effect.

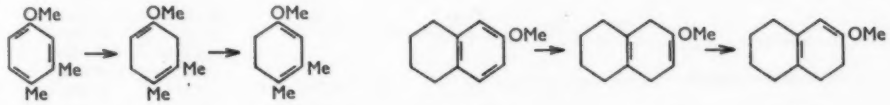
When the unconjugated diene (I) was isomerised for short periods (3 min. and 1 hr.), the product contained unchanged starting material together with the endo- and exo-cyclic dienes (II and III respectively), as shown by end absorption at 200—220 mμ and peaks at 268 and 244 mμ respectively. After 24 hours there was little end absorption and only one peak at 244 mμ, demonstrating complete conversion into the exocyclic diene (III). The infrared spectrum of the product showed a peak at 890 cm.$^{-1}$, probably due to the exocyclic methylene group, and the compound gave formaldehyde on ozonolysis.

By similar reactions, the unconjugated diene (IV; R = $CHMe_2$; R′ = R″ = H) obtained by reduction of 3-methoxy-*p*-cymene gave the corresponding exocyclic diene (VI), as did also the product (IV; R = R′ = H; R″ = Me) from 3-ethylanisole. On the other hand the compound (IV; R = R′ = R″ = Me), from 2-methoxy-*p*-cymene, gave only the corresponding endocyclic diene (V) and by use of more vigorous conditions,




(I) (II) (III) (IV) (V) (VI)

with lithium amide in boiling 1,2-diaminoethane, the same diene (V) was obtained together with some of the original aromatic compound. 3,4-Dimethylanisole (VII) and 1,2,3,4-tetrahydro-6-methoxynaphthalene (IX) also gave, finally, only the analogous dienes (VIII) and (X), respectively.



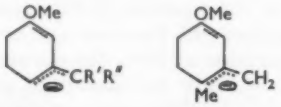

(VII) (VIII) (IX) (X)

The conversion of the endo- into the usually more stable (*transoid*) exo-cyclic diene presumably involves the production of intermediate salts of type (XI), and it has already been shown [4] that amide anion in liquid ammonia can cause isomerisation of some alkenes containing only one double bond. Failure of some endocyclic dienes to isomerise to the exocyclic isomers could be explained either by the greater stability of the former, which seems unlikely, or by inability to produce the appropriate anion. It has been shown [4] that the most readily isomerised alkenes are those containing the least number of alkyl substituents attached to the potential mesomeric system, a consequence, in part, of the inductive effect of the alkyl groups, but even more of steric inhibition of solvation of the anion. Such solvations clearly play a most important part in all reactions involving carbon anions, including reduction.[11] The favourable effect of liquid ammonia or related amines must be due largely to such solvation.

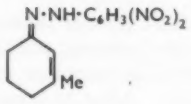
[8] Fieser and Fieser, "Steroids," Reinhold Publishing Corporation, New York, 1959, p. 16.
[9] O'Connor and Goldblatt, *Analyt. Chem.*, 1954, **26**, 1728.
[10] Woodward, *J. Amer. Chem. Soc.*, 1942, **64**, 72.
[11] Krapcho and Bothner-By, *J. Amer. Chem. Soc.*, 1959, **81**, 3658.

XUM

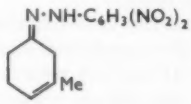
It appears therefore that an anion of type (XI) can be formed if R′ = R″ = H or R′ = H = R″ = Me but not if R′ = R″ = Me, in agreement with the above reasoning. The presence of an alkyl group at the other end of the potential mesomeric anion, as in system (XII), would explain the failure to isomerise in this case, although the endocyclic double bond might also be stabilised by the extra substitution. A similar explanation can be applied in the case of the hexahydromethoxynaphthalene.




(XI) (XII)




(XIII)




(XIV)

The 2,4-dinitrophenylhydrazones of the corresponding αβ- and βγ-unsaturated ketones, *e.g.*, (XIII) and (XIV), were prepared from the dihydroanisoles by known methods,[2,12] but attempts to prepare the pure 3-methylenecyclohexanone derivative from the exocyclic diene (III) failed, and this is obviously very readily isomerised to a 3-methylcyclohex-2-enone derivative.

## Experimental

Ultraviolet spectra were recorded with a Unicam S.P. 500 spectrophotometer for ethanol solutions, except in the cases of the dinitrophenylhydrazones, which were dissolved in chloroform.

The alkyldihydroanisoles, conjugated and unconjugated, are colourless liquids with a characteristic odour. Since the yields, apart from distillation losses, were almost quantitative in both reduction and conjugation reactions, they are not given below.

*Alkylanisoles.*—Where not already available, these were prepared by methylation of the phenol with dimethyl sulphate. In the following Table known values are given in parentheses for comparison.

Table 1.

| | B. p. | $n_D$ | λ (mμ) | $\varepsilon_{max.}$ |
|---|---|---|---|---|
| A. Anisole [a] | | | (270) | (1580) |
| | | | (277) | (1400) |
| B. 3-Methylanisole [a] | | | (272) | (1700) |
| | | | (278) | (1650) |
| C. 3-Ethylanisole | 110°/62 mm. | 1·5061/28° | 272 | 1810 |
| | | | 279 | 1730 |
| D. 3,4-Dimethylanisole | 105°/32 | 1·5129/30° | 278 | 1860 |
| | | | 284 | 1680 |
| E. 3-Methoxy-*p*-cymene | 94—95°/12 | 1·5050/23° | 275 | 2450 |
| | | | 281 | 2360 |
| F. 2-Methoxy-*p*-cymene | 100°/12 | 1·5068/22° | 274 | 2230 |
| | | | 280 | 2150 |
| G. 6-Methoxytetralin | 128—130°/13 | 1·5449/22° | 279 | 2180 |
| | | | 288 | 2030 |

[a] Burawoy and Chamberlain.[7]

*Reduction of Alkylanisoles.*—The compound (10 g.) was dissolved in liquid ammonia (500 ml.) and absolute alcohol (twice the theoretical amount required by the sodium used), and the solution was stirred mechanically in a 1 l. 3-necked flask provided with a solid carbon dioxide–acetone reflux condenser closed by a potassium hydroxide drying tube. Sodium (6—10 atom-equiv. calc. on the alkylanisole) was added in small pieces during 30—45 min. through the third neck, which was stoppered to avoid free access of air except during the actual additions, since oxygen competes for the metal.[13] The blue colour, at first fugitive, remained during

[12] Wilds and Nelson, *J. Amer. Chem. Soc.*, 1953, **75**, 5360.
[13] Eastham and Larkin, *J. Amer. Chem. Soc.*, 1959, **81**, 3652.

stirring for at least 30 min. after all the sodium had been added. Compounds which were difficult to reduce required greater atomic ratios of sodium (up to 10 atom-equiv.), and it was advisable to add enough of it to ensure that the blue colour remained for 1½ hr. after the end of the addition. In these cases, it was also preferable to use propan-2-ol instead of ethanol.

When the blue colour had disappeared (which result was readily obtained, if desired, by removal of the stopper for a few minutes), the condenser was removed and water (250 ml.) was added cautiously from a tap funnel with continued stirring. The product was extracted three times with light petroleum (b. p. 40—60°), the extract dried ($K_2CO_3$) and evaporated, and the residue distilled under water-pump vacuum. The reduction was repeated, if necessary, with propan-2-ol and a greater ratio of sodium, until the distillate had absorption in the 270—290 mμ range sufficiently small to indicate that the amount of unreduced compound was negligible (<3%).

The unconjugated products (see Table 2) gave no red colour with a solution of *p*-benzoquinone in benzene, but a black precipitate of quinhydrone resulted on gentle warming of the solution.[11]

*Isomerisation of Unconjugated Dienes.*—The unconjugated diene (7 g.) was added to a suspension of sodamide (from 1·7 g. sodium) in liquid ammonia (400 ml.), and the deep red solution, protected from ingress of air by a Bunsen valve, was set aside for 24 hr., during which the ammonia evaporated completely. More ammonia (100 ml.) was then added, followed by dropwise addition, with shaking, during 20 min., of a mixture of absolute ethanol (5 ml.) and ether (20 ml.), that destroyed the red colour. Water (200 ml.) was then added cautiously and the product extracted three times with light petroleum (b. p. 40—60°). After drying of the extract ($K_2CO_3$), the solvent was evaporated and the residue distilled under water-pump

TABLE 2.

| Cyclohexa-1,4-diene | Atom-equiv. of Na used | ROH | B. p./mm. | $n_D$ | Found (%) C | Found (%) H | Formula | Reqd. (%) C | Reqd. (%) H |
|---|---|---|---|---|---|---|---|---|---|
| A. 1-Methoxy- [1] ..... | 6 | EtOH | 45—46°/15 | 1·4775/24° | | | | | |
| B. 1-Methoxy-5-methyl- [1] | 6 | EtOH | 64°/16 | 1·4788/25° | | | | | |
| C. 1-*Methoxy*-5-*ethyl*- ... | 10 | Pr$^i$OH | 104—108°/42 | 1·4762/30° | 77·85 | 10·3 | $C_9H_{14}O$ | 78·2 | 10·2 |
| D. 1-*Methoxy*-4,5-*dimethyl*- ..... | 10 | Pr$^i$OH | 104—105°/40 | 1·4809/29° | 78·3 | 10·3 | ,, | ,, | ,, |
| E. 1-*Isopropyl*-2-*methoxy*-4-*methyl*- ..... | 9 | EtOH | 90°/12 | 1·4780/21° | 79·8 | 10·7 | $C_{11}H_{18}O$ | 79·5 | 10·8 |
| F. 1-*Isopropyl*-5-*methoxy*-4-*methyl*- ..... | 10 | Pr$^i$OH | 98—99°/16 | 1·4762/25° | 79·4 | 10·7 | ,, | ,, | ,, |
| G. 1,2,3,4,5,8-Hexahydro-6-methoxynaphthalene [11] ..... | 10 | Pr$^i$OH | 121—122°/14 | 1·5132/20° | | | | | |

TABLE 3.

| | B. p./mm. | $n_D$ | λ (mμ) | $\varepsilon_{max.}$ | Formula | | C (%) | H (%) |
|---|---|---|---|---|---|---|---|---|
| A. 1-Methoxycyclohexa-1,3-diene [4] | 42°/14 | 1·4893/24° | 268 | 4840 | | | | |
| B. 1-*Methoxy*-3-*methylenecyclohexene* | 62°/18 | 1·4929/23° | 244 | 5910 | $C_8H_{12}O$ | Found | 78·0 | 9·65 |
| | | | | | | Req. | 77·4 | 9·7 |
| C. 1-*Methoxy*-3-*ethylidenecyclohexene* | 118°/55 | 1·4902/26° | 247 | 5260 | $C_9H_{14}O$ | Found | 77·9 | 10·25 |
| | | | | | | Req. | 78·2 | 10·2 |
| D. 1-*Methoxy*-3,4-*dimethylcyclohexa*-1,3-*diene* | 99—100°/38 | 1·4866/28° | 271 | 3970 | ,, | Found | 78·2 | 10·35 |
| E. 3-*Isopropyl*-2-*methoxy*-6-*methylenecyclohexene* | 86—88°/12 | 1·4857/21° | 250 | 5050 | $C_{11}H_{18}O$ | Found | 79·45 | 10·8 |
| | | | | | | Reqd. | 79·5 | 10·8 |
| F. 2-*Isopropyl*-4-*methoxy*-5-*methylcyclohexa*-1,3-*diene* | 87—88°/12 | 1·4830/22° | 267 | 4230 | ,, | Found | 79·8 | 10·5 |
| G. 1,2,3,4,5,6-*Hexahydro*-7-*methoxynaphthalene* | 118—120°/13 | 1·5143/25 | 270 | 2470 | $C_{11}H_{16}O$ | Found | 80·3 | 10·0 |
| | | | | | | Reqd. | 80·5 | 9·75 |

vacuum. The resulting conjugated dienes (see Table 3) (both endo- and exo-cyclic) gave a red colour with a solution of *p*-benzoquinone in benzene.[11]

Similar experiments were carried out with the unconjugated dihydro-derivative of 3-methylanisole (Table 2; B) except that the isomerisation was allowed to proceed for (*a*) 3 min. and (*b*)

1 hr., before being stopped by rapid addition of alcohol (5 ml. in *ca.* 20 sec.), with shaking, followed by water. The products, obtained as before, both showed end-absorption in the region 200—220 mμ due to the original unconjugated diene, and flattened peaks at *ca.* 244 and 268 mμ., having ε values of 820 and 910 respectively in case (*a*) and both of 3200 in case (*b*), showing that the endo- and the exo-cyclic conjugated diene were formed in roughly equal and increasing amounts after isomerisation for 3 min. and 1 hr. respectively.

An attempt was made to obtain the exocyclic conjugated diene from unconjugated dihydrocarvacrol methyl ether (Table 2; F) by using more vigorous conditions. This compound (5·5 g.) and diaminoethane (50 ml., redistilled from sodium) were added to a suspension of lithium amide (from 0·8 g. of lithium) in liquid ammonia (100 ml.), and the mixture was gradually heated under a reflux water condenser until all the ammonia had evaporated. The diaminoethane solution was then boiled under reflux for 1 hr. After cooling, a mixture of ethanol (10 ml.) and ether (10 ml.) was added dropwise with shaking, followed by water (200 ml.), and the product (3·3 g.) was obtained as before. It showed end absorption in the ultraviolet region (perhaps due to tetrahydro-compound formed by disproportionation), and also peaks at 268, 273, and 280 mμ., the first of these being due to the conjugated endocyclic diene (Table 3; F) and the last two to the original aromatic compound (Table 1; F).

*Ozonolysis of 1-Methoxy-3-methylenecyclohexene.*—The compound (0·80 g.) in ethyl acetate (110 ml.) was ozonised at −80° and the solution then hydrogenated (uptake 2H) at room temperature and pressure over Adams catalyst (0·26 g.). After the catalyst had been filtered off, the filtrate was distilled into an excess of a saturated solution of dimedone in 10% aqueous alcohol, until about half of it had distilled. The mixture was boiled, with stirring, until the vapour no longer smelled of ethyl acetate, the remaining solution was cooled in ice, and the product was filtered off and dried. The formaldehyde–dimedone adduct (0·26 g.) had m. p. and mixed m. p. 188°.

*Preparation of 2,4-Dinitrophenylhydrazones.*—These were obtained by the methods of Wilds and Nelson.[13] The αβ-unsaturated ketone derivatives were obtained on boiling the unconjugated or conjugated (endo- or exo-cyclic) dienes with the reagent, whereas the βγ-unsaturated compounds were obtained from the unconjugated dienes by careful treatment in ice-cold solution. They were crystallised from alcohol except where otherwise stated, though use of light petroleum (b. p. 60—80°) was sometimes advantageous with the βγ-isomers.

αβ-Unsaturated 2,4-dinitrophenylhydrazones were obtained from:

B. 3-Methylcyclohex-2-enone, deep red plates, m. p. 175° (Birch [4] gives m. p. 174—175°).

C. *3-Ethylcyclohex-2-enone*, red needles, m. p. 165—166°, $\lambda_{max.}$ 388 mμ (ε 29,500) (Found: C, 55·25; H, 5·45; N, 18·3. $C_{14}H_{16}N_4O_4$ requires C, 55·25; H, 5·25; N, 18·4%).

D. 3,4-Dimethylcyclohex-2-enone, red needles, m. p. 149—150° (Birch [1] gives m. p. 146°), $\lambda_{max.}$ 389 mμ (ε 29,200) (Found: C, 55·5; H, 5·45; N, 18·35%).

E. 6-Isopropyl-3-methylcyclohex-2-enone (piperitone), orange-red needles, m. p. 116° (Birch and Mukherji [14] give m. p. 116°), $\lambda_{max.}$ 385 mμ (ε 28,200).

F. 3-Isopropyl-6-methylcyclohex-2-enone (carvenone), orange-red needles, m. p. 165° (Birch and Mukherji [14] give m. p. 165°).

βγ-Unsaturated *2,4-dinitrophenylhydrazones* were obtained from:

B. *3-Methylcyclohex-3-enone*, orange-red needles, m. p. 132—133°, $\lambda_{max.}$ 366 mμ (ε 24,000) (Found: C, 53·9; H, 4·8. $C_{13}H_{14}N_4O_4$ requires C, 53·8; H, 4·8%). This compound was reported by Lukes and Jizbu (*Chem. Listy*, 1952, **46**, 622) but the m. p. given (177—178°) shows that it was the αβ-unsaturated derivative.

D. *3,4-Dimethylcyclohex-3-enone*, orange-yellow hair-like [from light petroleum (b. p. 60—80°)], m. p. 143—144°, $\lambda_{max.}$ 366 mμ (ε 24,000) (Found: C, 55·6; H, 5·3. $C_{14}H_{16}N_4O_4$ requires C, 55·25; H, 5·25%).

E. *6-Isopropyl-3-methylcyclohex-3-enone*, orange-red needles, m. p. 119°, $\lambda_{max.}$ 368 mμ (ε 23,500) (Found: C, 58·1; H, 6·0; N, 16·9. $C_{16}H_{20}N_4O_4$ requires C, 57·8; H, 6·0; N, 16·7%).

F. *3-Isopropyl-6-methylcyclohex-3-enone*, orange-red needles, m. p. 155°, $\lambda_{max.}$ 368 mμ (ε 24,000) (Found: C, 58·1; H, 6·15. $C_{16}H_{20}N_4O_4$ requires C, 57·8; H, 6·0%).

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[*Received, June 27th*, 1961.]

[14] Birch and Mukherji, *J.*, 1949, 2531.

# 1060. *Physicochemical Properties of Some Chemotherapeutic Thioxanthones.*

By D. C. Munro.

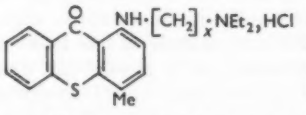
For Miracil D and three homologous compounds, the basicites have been measured and at pH 7·4 lipoid partition coefficients, surface activities, and protein affinities, which may be relevant to biological activity.

Many of the compounds used to combat the parasitic infections of malaria and schistosomiasis have structural features in common. The acridine and quinoline antimalarials mepacrine (Atebrin) and pamaquin (Plasmoquine), also the xanthone and thioxanthone drugs Miracil B and Miracil D (lucanthone), have each a reducible heterocyclic nucleus with an aliphatic diamine side-chain. It was the observation of a relation between acridines and xanthones which led Mauss [1] to the preparation of xanthones and thioxanthones, and hence to the discovery among the latter of activity against *Schistosoma haematobium* infections.

Properties such as basicity and reducibility, associated with the structural groupings common to all these compounds, may contribute to the activity against the different parasitic organisms. In fact some acridines are effective against *S. haematobium* infections. A series of thioxanthone compounds have been studied in a manner earlier applied to antimalarials, to see whether similar relations are to be found

In a series of investigations on acridine antimalarials, Hammick and Mason [2] measured several physicochemical parameters for correlation with antimalarial activity. The values of these parameters have now been found for the thioxanthone series which includes Miracil D (lucanthone; 1-2′-diethylaminoethylamino-4-methylthioxanthone hydrochloride) (I; $x = 2$).

Compounds homologous with Miracil D, and having three and four methylene groups in the side-chain (I; $x = 3$, 4), have been described by other workers,[1,3] who prepared them from the chloromethylthioxanthone by treatment with the diamine appropriate to the side-chain. The present work has made use of 1-amino-4-methylthioxanthone which was readily available in pure form from an earlier study; [4] and these compounds, together with the pentyl homologue (I; $x = 5$) have been prepared, but in small yield, by interaction of 1-amino-4-methylthioxanthone with the appropriate ω-bromoalkyldiethylamine hydrobromide.

(I) 


Miracil D and its homologues may be characterised as picrates. The hydrochlorides proved difficult to obtain with definite proportions of hydrogen chloride, the monohydrochlorides containing more than, and the dihydrochlorides less than, the stoicheiometric amount of acid. The monohydrochlorides were used for physical measurements, the uncertainty in concentration of the base, due to variable hydrogen chloride content in the salt, is less than 3%.

The importance of basicities in relation to various types of biological activity, exemplified by acridines, has been surveyed by Albert [5] for results obtained in water and in 50% aqueous ethanol.

Measurements have been made for Miracil D and its homologues, but the basicities of these thioxanthones cannot be measured in aqueous solution owing to the insolubility of the free bases. In 50% v/v ethanol, however, ~$10^{-3}$M-solutions of Miracil D base can be

[1] Mauss, *Chem. Ber.*, 1948, **81**, 19.
[2] Hammick and Mason, *J.*, 1950, 345, 348.
[3] Archer and Suter, *J. Amer. Chem. Soc.*, 1952, **74**, 4303.
[4] Hammick and Munro, *J.*, 1952, 1077.
[5] Albert, "The Acridines," Edward Arnold and Co., London, 1951, pp. 113—119, 251, 287, 298.

prepared; and the changes in apparent pH on addition of sodium hydroxide give a measure of the basicities. These are listed in the Table.

The basicities of the basic aromatic amino-group vary little, and the dissociation constants are little different from that of 1-amino-4-methylthioxanthone (apparent $pK_a$ 3·0). For the aliphatic basic centre, the values obtained show a progressive increase in basicity as the number of methylene groups separating the two basic centres is increased.

The values of $pK_a$ determined in 50% ethanol are generally about 0·8 unit (individually 0·43—1·46 unit) lower than those in water.[6] An acidity of pH 7·4, which is the mean acidity of the human bloodstream, appears therefore to correspond with an apparent pH of 8·2—8·3 in 50% ethanol.

Miracil D itself has apparent $pK_{a_2} = 8{\cdot}25$, while the homologous compounds have decidedly higher values. This suggests that substantial amounts of Miracil D are present as the free base in solution at pH 7·4, while the homologues are present as first conjugate acids.

This conclusion is supported by their behaviour in aqueous buffers without ethanol. At pH 7·4, $5 \times 10^{-5}$M-solutions of Miracil D slowly yielded crystals of the free base. Comparable solutions of the homologues did not do this, although from more alkaline solutions the free bases were precipitated.

Physicochemical properties of Miracil D series.

| Compound | Basicities in 50% EtOH $pK_{a_1}$ | $pK_{a_2}$ | Surface activities at $5 \times 10^{-5}$M $\gamma$ (dynes/cm.) | $\Delta\gamma$ | Protein affinity | Lipoid affinity |
|---|---|---|---|---|---|---|
| I; $x = 2$ (Miracil D) ..... | 3·4 | 8·25 | 71·12 | 2·46 | 1·0 | $9 \times 10^3$ |
| I; $x = 3$ ..... | 3·7 | 8·87 | 70·89 | 2·69 | 2·0 | $4 \times 10^3$ |
| I; $x = 4$ ..... | 3·5 | 9·22 | 68·40 | 5·18 | 1·9 | $4 \times 10^3$ |
| I; $x = 5$ ..... | 3·5 | 9·41 | 66·95 | 6·63 | 1·7 | $5 \times 10^3$ |
| 1-Amino-4-methylthioxanthone ... | 3·0 | — | — | — | — | — |

Surface activities and protein and lipoid affinities have been measured by procedures similar to those used by Hammick and Mason. The results do not relate to any single molecular species, but rather in each case to an equilibrium mixture of free base with its first conjugate acid; however, material in the bloodstream is present as a similar equilibrium mixture, and it is the properties of this mixture that are of significance in relation to therapeutic effect.

Surface activities have been assessed by the extent to which the compounds lower the surface tension of an aqueous buffer of pH 7·4. Values have been obtained by the drop-weight method. An increase in activity with chain length is observed, but owing to the presence in differing proportions of the first conjugate acid and the free base, the results do not agree well with Traube's rule, which suggests an approximately three-fold increase in surface tension lowering for each successive methylene group. The small difference between the surface activity of Miracil D and that of the first succeeding homologue may be accounted for by the relatively greater proportion of free base in the case of the former.

In the animal body, extraction of drugs from their centre of action by complex formation with proteins may be important in determining relative potencies. Wormall and Dewey [7] have indicated that complex formation with proteins may be assessed by precipitation methods. This, with the use of albumin as a representative protein, since it is quantitatively the major protein in blood plasma, provides the basis for a convenient laboratory method for assessment of protein affinities. Hammick and Mason [2] found that the precipitation method, applied to acridine antimalarials, gave results comparable with those from more elaborate dialysis procedures.

Solutions of Miracil D and homologues in phosphate buffer of blood pH were treated

[6] Albert and Goldacre, *J.*, 1946, 706.
[7] Wormall and Dewey, *Biochem. J.*, 1946, **40**, 119.

with a solution of blood albumin. After precipitation of albumin by addition of ethanol, approximately half the original amount of thioxanthone remained in solution. For each compound, the proportion of concentration remaining in solution related to the corresponding proportion measured for Miracil D gives the protein affinity in a form independent of the uncertain concentration of the albumin solution.

The ratios of extracted to residual concentration were of the same order as those observed by Hammick and Mason for acridine antimalarials. A minimum extraction of the compound with two methylene groups in the side-chain is observed, but there is little variation with side-chain length.

The partition coefficients between phosphate buffer of blood pH and acid-free oil have been determined in order to find the relative extents to which Miracil D and homologues may be extracted by fatty tissues in the body. Hammick and Mason used castor oil, which has a constitution sufficiently similar to that of animal fats and is liquid at room temperature; their procedure has been followed in studying the thioxanthone series.

Volumes of buffer containing known amounts of the thioxanthones were shaken with oil; after separation of the liquid layers the concentrations remaining in the aqueous layer were determined, and the partition coefficients calculated (Table 1). For the four compounds examined, the partition coefficients are high. A minimum extraction by oil is observed with the compounds having three and four methylene groups.

## Experimental

*Preparation of Solutions.*—Miracil D and its homologues, as monohydrochlorides, were dried for several days under a vacuum over sulphuric acid. Weighed quantities were dissolved in water to give $1{\cdot}6$—$2{\cdot}0 \times 10^{-3}$M-solutions. These were used in the titrations to find the basicities. Solutions in M/15-phosphate buffer of pH 7·4 (obtained by mixing M/15-$KH_2PO_4$, 1 vol. with M/15-$Na_2HPO_4$, 4 vol.) were prepared by diluting the aqueous solutions (5—10 ml.) with the volume of phosphate buffer (200—300 ml.) calculated to give $5 \times 10^{-5}$M-solutions. 1-Amino-4-methylthioxanthone hydrochoride was dissolved in ethanol to give a $2{\cdot}05 \times 10^{-3}$M-solution.

*Basicities.*—The solution (10 ml.) of the compound to be examined was treated with appropriate amounts of ethanol and water to give 50 ml. of solution containing 50% v/v of ethanol, and cooled to room temperature (18°). In the case of Miracil D and its homologues as monohydrochlorides, one equiv. of acid was added to give a solution equivalent to the dihydrochloride. A glass electrode was used to observe changes in pH after addition of successive small amounts of 0·02N-sodium hydroxide; stirring and protection from atmospheric carbon dioxide were provided by nitrogen bubbled through the liquid.

*Surface-tension Measurements.*—A stalagmometer of Pyrex glass, with a capillary air leak, had a drop time of 20 sec. The weights of 5 drops were found, for water, for M/15-phosphate buffer of pH 7·38, and for $5 \times 10^{-5}$M-solutions of Miracil D and its homologues in the phosphate buffer. Results were calculated on the basis of direct proportionality between surface tension and drop weight, with the value 72·75 dynes/cm. at 20° for the surface tension of water. The surface tension of the M/15-phosphate buffer solution was found to be 73·58 dynes/cm. at 20°.

*Protein Affinities.*—Blood albumin was obtained from B.D.H. Albumin (20 g.) with water (400 ml.) was stored for 3 days at 0—5°. Undissolved solid was removed by filtration and at the centrifuge. $5 \times 10^{-5}$M-Solutions of the thioxanthones in the M/15-phosphate buffer were employed; for Miracil D, a saturated solution (*ca.* $2{\cdot}2 \times 10^{-5}$M) was used. The thioxanthone in M/15-phosphate buffer (20 ml.) was mixed with the albumin solution (20 ml.); after 30 min. at room temperature, ethanol (40 ml.) was added and the precipitated material was removed by centrifugation (3500 r.p.m.), by boiling the solution, and by extraction of the thioxanthone by chloroform. The extract was evaporated to dryness, and the residue redissolved in 0·1N-hydrochloric acid (10 ml.). 2M-Sodium acetate (1·0 ml.) was added and the concentration of the thioxanthone estimated colorimetrically. Reference solutions were obtained from each initial solution of thioxanthone in the phosphate buffer by a parallel extraction procedure.

For each of the four homologues, the ratio (loss in concentration)/(residual concentration)

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was calculated. The protein affinities were obtained by dividing this ratio by that obtained for Miracil D.

*Lipoid Affinities.*—Castor oil (B.P.) was made acid-free by shaking a weighed quantity of oil with water and sodium carbonate (1 mol. per equiv. of acidity). The oil was recovered, after filtration, by extraction with ether; from the dried extract ether was removed by distillation and by heating the residue at 100°/15 mm.

Preliminary experiments were conducted in order to determine the initial concentration and the quantity of castor oil required to give a residual concentration in the aqueous layer of about $2 \times 10^{-5}$M.

A weighed quantity of acid-free oil (15—40 mg.; $d$ 0·963) and the solution (50 ml.) of the thioxanthone in M/15-phosphate buffer were shaken together for 2½ hr. The resulting emulsion was broken on the centrifuge at 3500 r.p.m. and the aqueous layer removed and filtered. The residual concentration in the aqueous layer was determined colorimetrically.

*Preparation of Thioxanthones.*—The homologues of Miracil D were prepared by heating 1-amino-4-methylthioxanthone [4] (1 mol.) with the ω-bromoalkyl-diethylamine hydrobromide (2 mol.) in ethanol for 96—168 hr. The product was separated from unchanged 1-amino-4-methylthioxanthone by 2N-hydrochloric acid, which precipitated the latter while retaining the diethylaminoalkylaminothioxanthone in solution: these were characterised as picrates.

The bromopropyldiethylamine hydrobromide was obtained from trimethylene dibromide.[8] For the two higher homologues tetrahydrofuran and tetrahydropyran, respectively, yielded the corresponding chloroalkyl acetates by treatment with acetyl chloride in the presence of zinc chloride;[9] on treatment with diethylamine and subsequent hydrolysis these gave the hydroxyalkyldiethylamines; distillation with hydrobromic acid yielded the bromoalkyldiethylamine hydrobromides.

1-2′-*Diethylaminoethylamino*-4-*methylthioxanthone picrate*, crystallised from ethanol, had m. p. 142° (Found: C, 55·1; H, 4·1; N, 12·6. $C_{20}H_{24}N_2OS,C_6H_3N_3O_7$ requires C, 54·8; H, 4·8; N, 12·3%). 1-3′-*Diethylaminopropylamino*-4-*methylthioxanthone picrate* (from ethanol) had m. p. 173·5° (Found: C, 55·9; H, 5·1; N, 12·0. $C_{21}H_{26}N_2OS,C_6H_3N_3O_7$ requires C, 55·6; H, 5·0; N, 12·0%). The monohydrochloride (from ethanol) had m. p. 173° (Mauss [1] gives m. p. 173°; Archer and Suter [3] give m. p. 164—165°) (Found: N, 6·9; Cl, 11·5. Calc. for $C_{21}H_{26}N_2OS,HCl$: N, 7·2; Cl, 9·1%). The hygroscopic dihydrochloride (from methanol and ether) had m. p. 148° (Found: Cl, 14·3. Calc. for $C_{21}H_{26}N_2OS,2HCl$: Cl, 16·6%). 1-4′-*Diethylaminobutylamino*-4-*methylthioxanthone picrate* (from ethanol) had m. p. 128·5° (Found: C, 56·4; H, 5·0; N, 11·8. $C_{22}H_{28}N_2OS,C_6H_3N_3O_7$ requires C, 56·3; H, 5·2; N, 11·7%). The monohydrochloride (from methanol–ether) had m. p. 201° (Found: N, 7·2; Cl, 10·1. Calc. for $C_{22}H_{28}N_2OS,HCl$: N, 6·9; Cl, 8·75%). The hygroscopic dihydrochloride (from methanol–ether) had m. p. 210° (Archer and Suter [3] give m. p. 153—155°) (Found: Cl, 13·4. Calc. for $C_{22}H_{28}N_2OS,2HCl$: Cl, 16·25%). 1-5′-*Diethylaminopentylamino*-4-*methylthioxanthone picrate* (from ethanol) had m. p. 134° (Found: C, 57·0; H, 5·1; N, 11·8. $C_{23}H_{30}N_2OS,C_6H_3N_3O_7$ requires C, 56·9; H, 5·4; N, 11·45%). The *monohydrochloride* (from ethanol) had m. p. 190° (Found: N, 6·35; Cl, 8·1. $C_{23}H_{30}N_2OS,HCl$ requires N, 6·7; Cl, 8·5%). The hygroscopic dihydrochloride (from methanol–ether) had m. p. 156° (Found: Cl, 13·8. Calc. for $C_{23}H_{30}N_2OS,2HCl$: Cl, 15·6%).

The author thanks Dr. Ll. Hammick, F.R.S., for his sustained interest and for helpful discussion.

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The University, Leeds, 2. [*Received, May* 31*st*, 1961.]

[8] Marvell, Zartman, and Bluthardt, *J. Amer. Chem. Soc.*, 1927, **49**, 2301.
[9] Cloake and Pilgrim, *J. Amer. Chem. Soc.*, 1939, **61**, 2667.

## 1061. *The Adsorption of Water Vapour by Lecithin and Lysolecithin, and the Hydration of Lysolecithin Micelles.*

By P. H. Elworthy.

The adsorption of water vapour by lecithin, lysolecithin, triolein, and tristearin has been studied at 25° and 40°. The polar parts of the phosphatide molecules appear to be responsible for adsorption, and the results were fitted by B.E.T. plots at low relative vapour pressures. Some hysteresis in the adsorption isotherms was found for lysolecithin. Certain thermodynamic quantities have been calculated from the adsorption results. A value of micellar hydration of lysolecithin has been calculated from transport properties of solutions, and compared with the value found from adsorption experiments.

The adsorption of water vapour by proteins has been studied by several authors.[1,2] No reports have been made of adsorption by phosphatides and, in view of their biological importance, it was considered worthwhile to study the uptake of water vapour by these substances.

As the phosphatides form part of the animal cell membrane, the extent of their hydration may well influence the adsorption of drugs on to the membrane, and also the passage of biologically active materials through it. Choline, which is intensely hygroscopic, is present in the molecules of both lecithin and lysolecithin, indicating that the polar parts of the phosphatide molecules would be responsible for adsorption of water vapour. Adsorption studies should give an idea of the extent of hydration of phosphatide micelles.

A second line of approach to micellar hydration is to use the transport properties of the phosphatides in solution to obtain values of micellar weight, which can be compared with a value found from light scattering; as the micelles of lysolecithin are reasonably spherical, discrepancies between the two values of micellar weight are likely to be due to hydration. The extent of hydration can thus be calculated.

### Experimental

*Materials.*—Lecithin was prepared from the mixed phosphatides of chicken's egg yolks by treatment with alumina to remove ninhydrin-reacting materials, followed by chromatography on silica to remove lysolecithin.[3] Lysolecithin was prepared from the lecithin–lysolecithin mixture obtained after the alumina treatment by Saunders's method.[4] Two samples of each material were used. Two samples of lecithin contained, respectively, N 1·77, 1·75, and P 3·92, 3·83%, and had I no. 55, 73. Two samples of lysolecithin contained, respectively, N 2·62, 2·65 and P 5·80, 5·90% and had I nos. 8.

Glycerol trioleate and tristearate were " molecularly " distilled, the former having I no. 83 (calc., 86) and the latter m. p. 70° (lit.,[5] 72°).

The sulphuric acid used was of " AnalaR " quality.

*Adsorption of Water Vapour.*—The phosphatide was contained in a weighing bottle over a solution of sulphuric acid under a vacuum. At the beginning of each experiment the flask containing the acid and weighing bottle was placed in carbon dioxide–ether and evacuated at 0·01 mm. for 2 hr., allowed to warm at intervals, and recooled. It was then placed in a thermostat bath at 25° or 40° (±0·01°). The sample was weighed every 24 hr. until its weight was constant. Equilibrium was nearly always reached within 1 day and, at longest, 48 hr.

[1] Altman and Benson, *J. Phys. Chem.*, 1960, **64**, 851; Mellon, Horn, and Hoover, *J. Amer. Chem. Soc.*, 1947, **69**, 827; 1948, **70**, 1144, 3040; 1949, **71**, 2761.
[2] Bull, *J. Amer. Chem. Soc.*, 1944, **66**, 1499.
[3] Elworthy and Saunders, *J.*, 1957, 330.
[4] Saunders, *J. Pharm. Pharmacol.*, 1957, **9**, 834.
[5] Heilbron and Bunbury, " Dictionary of Organic Compounds," Eyre and Spottiswoode, London, 1953, Vol. IV, p. 633.

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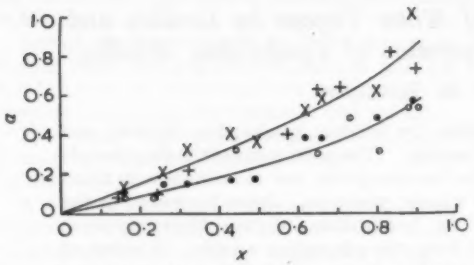


FIG. 1. Adsorption of water vapour by triolein at 40° (×) and at 25° (+) and by tristearin at 40° (•) and at 25° (○). $a$ = g. of water adsorbed per 100 g. of phosphatide, and $x$ = relative vapour pressure (also for other Figures).

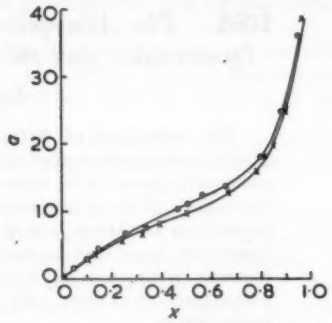


FIG. 2. Adsorption of water vapour by lecithin at 40° (○) and at 25° (×).

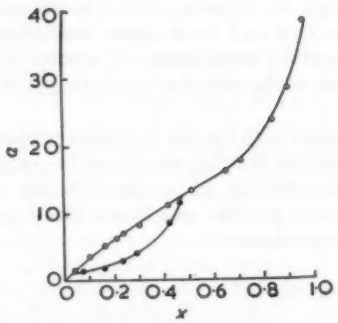


FIG. 3. Adsorption of water vapour by lysolecithin at 25°: • adsorption, ○ desorption.

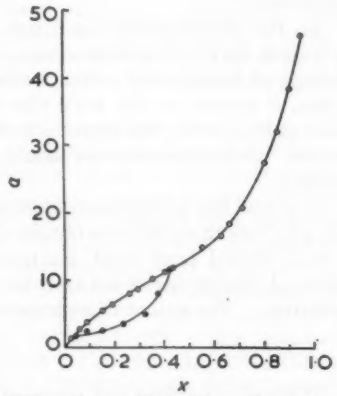


FIG. 4. Adsorption of water vapour by lysolecithin at 40°: • adsorption, ○ desorption.

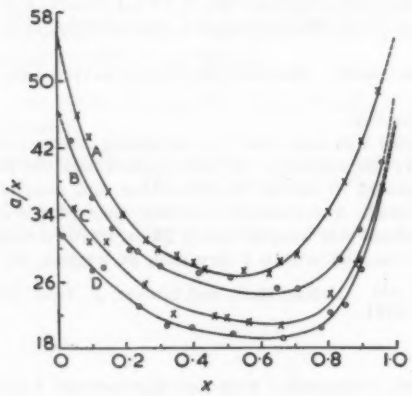


FIG. 5. Graphs of $a/x$ against $x$ for lecithin and lysolecithin.

Lysolecithin at (A) 40° and (B) 25°.
Lecithin at (C) 40° and (D) 25°.

The concentration of sulphuric acid solution was determined by titration. A loose flap of Polythene was placed across the neck of the weighing bottle to prevent water droplets falling in when the vacuum was released at the end of a run. Corrections for small loss on drying were obtained for the phosphatide samples by drying them at 60°/0·01 mm. The weights of the samples plus adsorbed water were reproducible to ±0·3 mg.

The results of the adsorption experiments are shown in Figs. 1—4. There is considerable scatter of results for tristearin and triolein, owing to the small amounts of water vapour taken up (at a relative vapour pressure of 0·91, tristearin adsorbed only 5·6 mg. of water per g.). For these substances adsorption appeared to be independent of temperature. No differences in adsorptive power were observed between the samples of lecithin or of lysolecithin used. For lecithin, triolein, and tristearin, the amount adsorbed was independent of the way in which equilibrium was reached, *i.e.*, from under- or over-saturation. Lysolecithin gave hysteresis loops (Figs. 3 and 4) between relative vapour pressures ($x$) of 0·05 and 0·5. The adsorption isotherm for the phosphatides is S-shaped; this type has also been observed for proteins.[1,2] More water vapour was adsorbed at higher than at lower temperatures.

Fig. 5 gives a plot of $a/x$ against $x$, where $a$ is g. of water per 100 g. of phosphatide. This plot allows extrapolation to $x = 0$ and $x = 1$, and was used for the calculation of some thermodynamic quantities and for determination of water-vapour uptake at saturation.

The results on phosphatides gave good B.E.T.[6] plots below a relative vapour pressure of 0·5. In the Table, $a_1$, $a_2$, and $a_8$ are the amounts of water vapour adsorbed in first layer, second layer, and at saturation, respectively, in g. of water per 100 g. of phosphatide. Figures in parentheses give the $a$ value in terms of moles of water per mole of phosphatide.* $C$ is the B.E.T. constant. Although $a_1$ is larger for lysolecithin than for lecithin on a weight basis, this is reversed when the amount adsorbed is calculated as mole/mole. Water adsorbed in excess of $a_1$ corresponds to the moderately linear portion of the adsorption isotherms (Figs. 2—4) between $x = 0{\cdot}25$ and $x = 0{\cdot}55$. The points where the isotherms start their upward swing can be determined from Fig. 5, and these values are given as $a_2$ in the Table. They are roughly twice the $a_1$ figures. Above $a_2$, the amount of water vapour adsorbed increases very sharply, and $a_8$ was determined from Fig. 5.

Constants from B.E.T. plots on lecithin and lysolecithin.

| | $a_1$ | $a_2$ | $a_8$ | $C$ |
|---|---|---|---|---|
| Lecithin at 25° | 5·63 (2·50) | 12 (5·1) | 44 (19·5) | 7·71 |
| Lecithin at 40° | 6·12 (2·71) | 14 (6·0) | 48 (21) | 9·63 |
| Lysolecithin at 25° (Desorb) | 8·05 (2·37) | 17 (5·0) | 48 (14) | 6·16 |
| Lysolecithin at 40° (Desorb) | 8·20 (2·42) | 15 (4·5) | 55 (16) | 7·30 |

## Discussion

Any interpretation of the adsorption of water vapour requires some knowledge of the molecular structure of solid lecithin and lysolecithin. *X*-Ray diffraction studies on lecithin [7] showed that the molecules were arranged in bimolecular leaflets, the polar groups forming the outer surfaces of the leaflets, and the hydrocarbon chains being parallel to one another on the inside. This type of structure also appears to be present in lecithin micelles in aqueous solution. No *X*-ray diffraction studies have been made on lysolecithin, but it seems reasonable to assume that a roughly similar structure to that of lecithin exists in the solid.

Compared with lecithin and lysolecithin, triolein and tristearin adsorb only very small amounts of water vapour (Fig. 1), indicating that the phosphorylcholine part of the phosphatide molecule is principally responsible for adsorption. Triolein, containing double bonds, adsorbs slightly more than tristearin, but the effect is small. The adsorption of water vapour can therefore be expected to take place around the polar head groups of the phosphatide molecules. From the value of $a_1$ in Table 1, there are 2·5—2·7 molecules of water adsorbed on each head group of lecithin and 2·4 molecules for lysolecithin, the exact

* The molecular weights of phosphatides were calculated from nitrogen and phosphorus contents.

[6] Brunauer, Emmett, and Teller, *J. Amer. Chem. Soc.*, 1938, **60**, 309.
[7] Baer, Palmer, and Schmitt, *J. Cell. Comp. Physiol.*, 1941, **17**, 355.

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values depending on temperature. Using 10·5 Å² as the area of the water molecule [8] gives head group areas of 26—28 and 25 Å², respectively. As might be expected of allied molecules containing the same polar group which is responsible for the adsorption, these values are similar. Molecular models give a head group area of 60—65 Å² and surface film [9] studies 80—100 Å². Generally, the surface areas of proteins measured from the adsorption of water vapour are too small,[2] and the same appears to be true for phosphatides.

The completion of the second layer roughly doubles the amount of water adsorbed, and there are now about five water molecules associated with each phosphatide head group. The adsorption is a complex process and there are several interpretations of the way it could occur. Opposing head groups, one on each side of the gap between the bimolecular leaflets, may share the water molecules between them, giving approximately ten molecules between two head groups at the completion of the second layer. Alternatively each individual phosphatide molecule might conduct its adsorption independently of its neighbour. There might be adsorption into cavities on the phosphorylcholine group in this process. Calculations based on the transport properties of lysolecithin in solution suggest that cavities might play a part for this compound (see below).

Continued uptake of water vapour expands the gap between the bimolecular leaflets and gives a colloidal solution at saturation in which the leaflets are detached from one another. It is interesting that, mole/mole, lecithin adsorbs more water vapour than lysolecithin at saturation, although the latter is freely soluble in water while the former is only dispersible. This effect may be allied to the differences of micellar structure in solution. Several differences were found between the two phosphatides in the adsorption studies: in the amounts of water adsorbed, in the B.E.T. constant $C$, and in the presence of a hysteresis loop for lysolecithin. The exact spatial arrangements of the phosphorylcholine group, while being generally similar, may not be exactly the same in the two compounds, causing the ease of access of water vapour to this group to differ. The desorption isotherms are alike in general shape, indicating that the removal of water from the gap between the leaflets is a similar process for each substance.

An idea of the affinity of solid adsorbent for water vapour can be obtained by calculating the free energy required to transfer one mole of vapour from the vapour state to the solid surface.[2] Such calculations were made with the aid of the plots of $a/x$ against $x$ (Fig. 5) and show that the affinity of lecithin for water vapour is higher than that of lysolecithin on a mole/mole basis; this again indicates some difference between the interactions of water vapour with the two compounds.

*Transport Properties of Lysolecithin.*—A further insight into the hydration of lysolecithin may be gained by considering properties of its solutions. Saunders and Thomas [10] reported the diffusion coefficient at 25° as $6{\cdot}544 \times 10^{-7}$ cm.² sec.$^{-1}$. Robinson and Saunders [11] gave the density as 1·021 g. ml.$^{-1}$. If the micelle is assumed to be spherical and unhydrated, these results give a micellar weight of 136,000 from the Stokes–Einstein equation. Light-scattering studies [12] showed that the micelles were reasonably spherical (observed dissymmetries close to unity, and small depolarisations) and that the micellar weight was 97,000. The discrepancy between the two values of the micelle size is likely to be due to the hydration of the micelle, causing the observed diffusion coefficient to be smaller than expected.

By taking the light-scattering molecular weight as that of an unhydrated sphere, the diffusion coefficient ($D_0$) can be calculated as $7{\cdot}317 \times 10^{-7}$ cm.² sec.$^{-1}$. The ratio of the

[8] Brunauer, " Physical Adsorption of Gases and Vapours," Oxford Univ. Press, 1945, p. 287.
[9] Hughes, *Biochem. J.*, 1935, **29**, 430; Alexander and Teorell, *Trans. Faraday Soc.*, 1939, **35**, 727; Cheesman, *Arkiv Kemi, Min., Geol.*, 1946, **22**, *B*, No. 1.
[10] Saunders and Thomas, *J.*, 1958, 483.
[11] Robinson and Saunders, *J. Pharm. Pharmacol.*, 1959, **11**, 304.
[12] Robinson, Thesis, London, 1959, p. 41.

frictional coefficient ($f$) of the hydrated micelle to that of the unhydrated micelle ($f_0$) is related to the ratio of the diffusion coefficients by

$$f/f_0 = D_0/D, \quad (1)$$

giving $f/f_0 = 1{\cdot}118$.

Oncley [13] gives a relation between the ratio of the frictional coefficients and the extent of hydration ($w$)

$$f/f_0 = (1 + w/\bar{v}\rho)^{\frac{1}{3}} \quad (2)$$

where $\bar{v}$ is the specific volume of solute, and $\rho$ is the density of solvent. From equation 3, $w =$ 0·39 g. of water per g. of lysolecithin. The accuracy of this estimate will not be high, as the diffusion coefficient will have an error of approximately $\pm 1\%$, while Saunders and Robinson [14] assessed the error of their light-scattering molecular weight as $\pm 7\%$. However, the agreement between this value for the hydration, and that obtained from the water-vapour experiments, 0·48 g. of water per g. of lysolecithin, is reasonable.

A further value of micellar hydration can be obtained from results of viscosity experiments on lysolecithin.[15] The intercept of a graph of $\eta_{sp}/\phi$ against $\phi$ gave $(\eta_{sp}/\phi)_{\phi=0} = 3{\cdot}9$, where $\eta_{sp}$ = specific viscosity and $\phi$ = volume fraction of solute. For unhydrated spherical particles the intercept should be 2·5. From the larger value found experimentally for hydration, $w$ takes [13] the value of 0·58 g. of water per g. of lysolecithin, again in reasonable agreement with the other values.

In attempts to decide whether the hydrating water forms a unimolecular layer around the micelle, the most accurate experimental result, the diffusion coefficient, is used to calculate the micellar radius of 37·5 Å. In a simple model of the micelle, the centres of the water molecules will be on a plane of distance (radius micelle—radius water molecule, considered as a sphere) from the centre of the micelle. A unimolecular film of water in this position around the micelle gives 0·28 g. of water per g. of lysolecithin for the hydration, which is much less than the estimates from the other methods. Assuming a bimolecular layer we have 0·50 g. of water per g. of lysolecithin. There is a serious drawback to the second assumption, in that the radius of the micelle remaining for occupation by lysolecithin molecules is only 30 Å$^2$, which is much smaller than the length of the lysolecithin molecule, as measured from molecular models.

Probably the hydration of the micelle consists of two distinct parts: first, a unimolecular layer of water as a sheath around the micelle; secondly, water which possibly hydrates the charged head group. An estimate of the second quantity can be obtained by subtracting the quantity present in the unimolecular layer from the mean estimate of the total hydration, *i.e.*, $(0{\cdot}48 + 0{\cdot}39 + 0{\cdot}58)/3 - 0{\cdot}28 = 0{\cdot}20$ g. of water per g. of lysolecithin. Examination of a model of the micelle shows that the polar head group is not flat, but may contain considerable cavities capable of holding water in position close to the nitrogen and phosphorus atoms. It is interesting that 0·17 g. of water per g. of lysolecithin was the amount required to complete the second layer in the water-vapour adsorption process. It may be that the first and the second layer of adsorption represent the hydration of the polar groups, and the remaining uptake occurs in separation of the bimolecular leaflets.

Calculations of the hydration of lecithin micelles from properties of its solutions are not possible, as their diffusion coefficients have not been determined and the interpretation will be complicated by the asymmetry of the micelles.[16] An approach is being made to this problem by using synthetic lecithin.

I thank Miss M. Buchanan for technical assistance.

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Glasgow, C.1. [*Received, June 5th*, 1961.]

[13] Oncley, *Ann. N.Y. Acad. Sci.*, 1940—1941, **41**, 121.
[14] Robinson and Saunders, *J. Pharm. Pharmacol.*, 1959, **11**, 115T.
[15] Robinson, Thesis, London, 1959, p. 46.
[16] Robinson, *Trans. Faraday Soc.*, 1960, **56**, 1260.

## 1062. *Initial Thermoelectric Power Measurements on Thermocells with Iodine–Iodide Electrodes at a Mean Temperature of* 30°.

By H. J. V. Tyrrell and P. J. Wilson.

Thermocells with iodine–iodide electrodes give very reproducible values of initial thermoelectric powers. An equation relating this quantity to the iodine and iodide concentrations in the cell is derived, together with a simple extrapolation procedure to eliminate the entropy of transfer of the complex tri-iodide ion. This has been tested for a series of iodides with univalent cations, and the extrapolation errors shown to be small. The experimental data have been used to compute values of the Soret coefficients of the iodides studied relative to that of one iodide selected as a standard. These are consistent with some recent direct measurements of Soret coefficients by a conductimetric method. The standard transported entropy of the iodide ion, apart from a small correction term, has been calculated to be 27·4 cal. g.-ion$^{-1}$ deg.$^{-1}$ which agrees quite well with the value of 28·1 units obtained by Haase, Hoch, and Schönert from data on silver–silver iodide thermocells.

Experimental data on the initial thermoelectric power ($\varepsilon_0$) of thermocells can be used to calculate relative values of Soret coefficients for a series of salts having a common ion.[1] Such calculations depend on the determination of small differences between $\varepsilon_0$ values for thermocells having the same electrodes but different electrolytes; these may be no more than a few microvolts per degree and accurate values of $\varepsilon_0$ are needed. Silver–silver halide electrodes have been most commonly used in studies on thermocells but they are not ideal for the purpose. A redox electrode in which the electron-transfer process takes place between two dissolved species should in principle be more reproducible, and it is known that measurements of extreme precision are possible with the platinum–iodine–iodide electrode.[2] When this work began the best available Soret coefficient measurements on dilute alkali iodide solutions were those due to Alexander,[3] obtained at a mean temperature of 30°. Accordingly, measurements on thermocells containing these electrodes have been carried out at this mean temperature with electrolytes prepared from a number of univalent iodides.

The thermocell can be written:

| Pt ——— Pt | Solution of MI, and iodine | Pt ——— Pt |
|---|---|---|
| $T_0$ $T$ | | $T + \Delta T$ $T_0$ |

the electrode reactions being,

$$I^- \longrightarrow \tfrac{1}{2}I_2 + \varepsilon^- \text{ at } T \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (a)$$

$$\tfrac{1}{2}I_2 + \varepsilon^- \longrightarrow I^- \text{ at } T + \Delta T \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (b)$$

if the right-hand (heated) electrode is taken as positive. $T_0$ is the temperature of the potentiometer terminals. It is not difficult to show[4] that, if the temperature interval is small, the initial thermoelectric power, $\varepsilon_0$, of this cell is given by

$$F\varepsilon_0 = -S^*_{\text{el. Pt}} + \Delta S_R - \sum_k t_k S^*_k/z_k \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

$S^*_{\text{el. Pt}}$ is the entropy of transfer of the electron in the platinum conductor, and $\Delta S_R$ the

[1] *E.g.*, Tyrrell and Hollis, *Trans. Faraday Soc.*, 1952, **48**, 893; Tyrrell and Colledge, *ibid.*, 1954, **50**, 1056.

[2] *E.g.*, MacInnes and Dayhoff, *J. Chem. Phys.*, 1952, **20**, 1034; Agar and Breck, *Nature*, 1955, **175**, 298.

[3] Alexander, *Z. phys. Chem.* (*Leipzig*), 1954, **203**, 213.

[4] *E.g.*, Tyrrell, "Diffusion and Heat Flow in Liquids," Butterworth, London, 1961.

entropy change in the reaction (*b*). $S^*_k$ and $z_k$ are respectively the entropy of transfer and valency of the ion species k, the sum being taken over all the ion species present. By definition,

$$\Delta S_R = s_{I^-} - \tfrac{1}{2}s_{I_2} - s_{\text{el. Pt}}$$

and

$$s_{I^-} = s^\circ_{I^-} - \boldsymbol{R} \ln a_{I^-} - \boldsymbol{RT}\ \partial/\partial T\ (\ln a_{I^-})$$

$$s_{I_2} = s^\circ_{I_2} - \boldsymbol{R} \ln a_{I_2} = \boldsymbol{RT}\ \partial/\partial T\ (\ln a_{I_2})$$

where $s_j$, $s^\circ_j$ are respectively the partial molar entropy, and the standard partial molar entropy of the species j. Inserting these values into equation (1), it follows that

$$\boldsymbol{F}\varepsilon_0 = -\bar{\bar{S}}_{\text{el. Pt}} + (s^\circ_{I^-} - \tfrac{1}{2}s^\circ_{I_2}) - \boldsymbol{R} \ln (a_{I^-}/a^{\frac{1}{2}}_{I_2}) - \boldsymbol{RT}\ \partial/\partial T \ln (a_{I^-}/a^{\frac{1}{2}}_{I_2}) - \sum t_k S^*_k/z_k. \quad . \quad (2)$$

$\bar{\bar{S}}_{\text{el. Pt}}$ is the transported entropy of the electron in the platinum conductor, defined as $(S^*_{\text{el. Pt}} + s_{\text{el. Pt}})$, and the activity terms refer to the *free* iodine and iodide ions. The solutions also contain the complex ion $I_3^-$ as the only complex species present when the iodine : iodide ratio is as small as in the present experiments. It is convenient to eliminate the activity of free iodine from equation (2) by introducing the association constant $\beta_1$:

$$\beta_1 = a_{I_3^-}/a_{I_2}a_{I^-}. \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

From (3),

$$\boldsymbol{R} \ln (a_{I^-}/a^{\frac{1}{2}}_{I_2}) + \boldsymbol{RT}\ \partial/\partial T \ln (a_{I^-}/a^{\frac{1}{2}}_{I_2}) = \frac{\boldsymbol{R}}{2} \left(\ln \frac{m^3_{I^-}}{m_{I_3^-}} + T\ \partial/\partial T \ln m^3_{I^-}/m_{I_3^-} + \ln \beta_1 + T\ \partial/\partial T\ .\ \ln \beta_1\right) + \boldsymbol{R}(\ln \gamma_{I^-} + T\partial/\partial T\ .\ \ln \gamma_{I^-}), \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

where $\gamma_{I_3^-}$ has been taken as equal to $\gamma_{I^-}$, and $m_j$ is the molality of species j. $\beta_1$ is of the order of $10^3$ l. mole$^{-1}$, and in these experiments the ratio (total iodine) : (total iodide) never exceeded 0·1. The free iodine concentration was thus always negligible, and it is legitimate to write

$$m_{I^-} = [I^-] - [I_2] \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

and

$$m_{I_3^-} = [I_2], \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (6)$$

where $[I^-]$, $[I_2]$, are respectively the total iodide and total iodine concentrations (molalities) in the solution. The change in the ratio of the concentrations of free iodide and of tri-iodide due to the shift in equilibrium with temperature is negligible in the experimental conditions, and all thermoelectric-power measurements were made before concentration gradients due to the Soret phenomenon could be established. Hence the term including $\partial/\partial T\ .\ \ln (m^3_{I^-}/m_{I_3^-})$ can be omitted from (4). Furthermore, $\boldsymbol{R}(\ln \beta_1 + T\ .\ \partial/\partial T\ .\ \ln \beta_1)$ is $\Delta S^\circ$, the standard entropy change in the association process which has the form:

$$\Delta S^\circ = s^\circ_{I_3^-} - s^\circ_{I_2} - s^\circ_{I^-} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (7)$$

From equations (2), and (4)—(7),

$$\boldsymbol{F}\varepsilon_0 + \frac{\boldsymbol{R}}{2} \ln ([I^-] - [I_2])^3/[I_2] + \boldsymbol{R}(\ln \gamma_{I^-} + T\ .\ \partial/\partial\ T\ .\ \ln \gamma_{I^-}) = -\bar{\bar{S}}_{\text{el. Pt}} + s^\circ_{I^-} - \tfrac{1}{2}(s^\circ_{I_3^-} - s^\circ_{I^-}) - \sum_k t_k S^*_k/z_k \quad . \quad . \quad . \quad . \quad (8)$$

For a given iodide concentration, the activity coefficient terms are substantially independent of the iodine concentration, and changes in the function $(\boldsymbol{F}\varepsilon_0 + \frac{\boldsymbol{R}}{2} \ln ([I^-] - [I_2])^3/[I_2])$, which are in practice small and arise mainly from the entropy of transfer

terms, do not prevent extrapolation of values of this function, measured at constant iodide but varying iodine concentrations, to zero iodine concentration; this extrapolated value can be denoted by $P_{\varepsilon,0}$. For an iodide MI, the Soret coefficient $\sigma_{MI}$, defined as shown, is related to ionic entropies of transfer by

$$\sigma_{MI} = -\left(\frac{d}{dT} \ln m\right)_{stat} = \frac{S^*_{M^+} + S^*_{I^-}}{2RT\,(1 + \partial \ln \gamma_{\pm 1}/\partial \ln m)_{T,P}}, \quad . \quad . \quad . \quad (9)$$

the suffix denoting that the concentration gradient is measured in the stationary state. Equation (8) then becomes,

$$FP_{\varepsilon,0} + R(\ln \gamma_{I^-} + T \,.\, \partial/\partial T \,.\, \ln \gamma_{I^-}) = \bar{\bar{S}}^\circ_{I^-} + \Delta S^*_{I^-} - \bar{\bar{S}}_{el.\,Pt} - \tfrac{1}{2}(s^\circ_{I_2} - s^\circ_{I^-}) - 2t_M RT\,(1 + \partial \ln \gamma_\pm/\partial \ln m)_{T,R}\sigma_{MI} \quad . \quad (10)$$

$\bar{\bar{S}}^\circ_{I^-}$ is the standard transported entropy of the iodide ion, that is, the sum of the standard molar entropy and the entropy of transfer in an infinitely dilute solution, and $\Delta S^*_{I^-}$ is the difference between the entropy of transport of the iodide ion in the solution considered and in an infinitely dilute solution.

For a second iodide, NI, the extrapolated thermoelectric power can be denoted by $P'_{\varepsilon,0}$, and the Soret coefficient by $\sigma_{NI}$. For dilute solutions, $\ln \gamma_{I^-}$, $\Delta S^*_{I^-}$ will be almost independent of the cation species and, from (9) and (10), for measurements taken in solutions of the same ionic strength,

$$\Delta P_{\varepsilon,0} = P_{\varepsilon,0} - P'_{\varepsilon,0} = -\frac{2RT}{F}\left\{t_M\left[1 + \left(\frac{\partial \ln \gamma_\pm}{\partial \ln m}\right)_{T,P}\right]_{MI} \cdot \sigma_{MI} - t_N\left[1 + \left(\frac{\partial \ln \gamma_\pm}{\partial \ln m}\right)_{T,P}\right]_{NI} \cdot \sigma_{NI}\right\} \quad . \quad . \quad (11)$$

*Experimental.*—The cell used was basically that used by Tyrrell and Hollis,[1] modified to take account of the tendency of iodine to distil out of the solutions during the measurements by extending the thermostat jackets above the closures on each side of the cell (Fig. 1). The

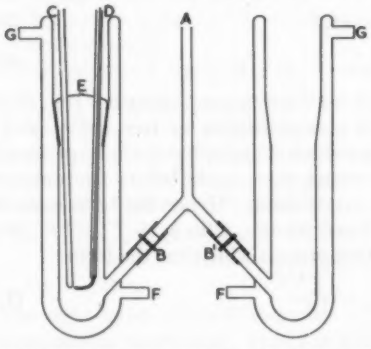


FIG. 1. Modified thermocell for iodine–iodide electrodes.

A, to manostat; B, B′ screw clips; C, thermocouple pocket; D, platinum electrode and lead; E, air leak; F, inlets to constant-temperature jackets; G, exits from constant-temperature jackets.

The right-hand side of the cell is not shown complete.

liquid junction was made in the inverted Y tube by releasing the air pressure at A after the screw-clips on the short lengths of silicone rubber tubing had been opened at B,B′. The temperature interval between the two half-cells was measured with two single copper–constantan thermocouples which had been calibrated by means of the secondary fixed points provided by the sodium chromate decahydrate–hexahydrate transition [5] and the sodium sulphate decahydrate–anhydrous sodium sulphate transition.[6] The e.m.f.s on the thermocell and on the thermocouples were measured on a Cambridge Vernier potentiometer.

Solutions of iodine in the appropriate iodide, with ionic strengths of approximately 0·2, 0·1,

[5] Richards and Kelly, *J. Amer. Chem. Soc.*, 1911, **33**, 847.
[6] Dickinson and Mueller, *J. Amer. Chem. Soc.*, 1907, **29**, 1381.

and 0·05m, and iodine concentrations between $2 \times 10^{-2}$ and $10^{-4}$ m. were prepared, and the compositions checked by weight titration. The elementary iodine was determined directly by titration with sodium arsenite, and the iodide by oxidising it to iodine and then determining the total iodine by a similar titration. The iodides used were of the purest available grade, and were purified by recrystallisation except in the case of ammonium iodide where Smith and Eastlack's method [7] was used.

*Results and Discussion.*—It follows from equation (8) that, for a particular concentration of a given salt, the quantity, $\varepsilon_0 + \frac{R}{2F} \ln ([I^-] - [I_2])^3/[I_2]$, will change with the iodine : iodide ratio only to the extent that the term $\sum_k t_k S^*_k/z_k F$ changes, provided that the assumptions made in the derivation of eqn. (8) are correct. In Fig. 2 this quantity is plotted against the iodine : iodide ratio for different iodide solutions. Errors in the

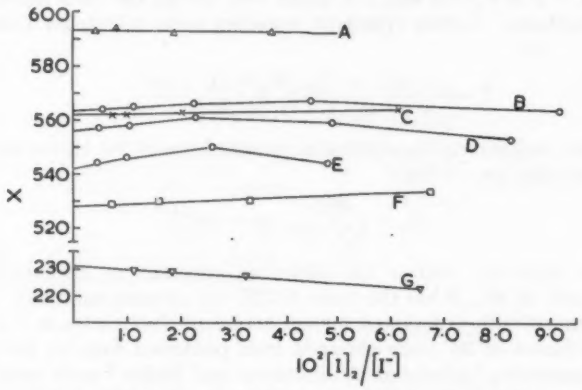


FIG. 2. Extrapolation of thermocell data to zero iodine concentration. The ordinate (X) records $\varepsilon_0 + \frac{R}{2F} \ln ([I^-] - [I_2]^3)/[I_2]$ ($\mu$v deg.$^{-1}$).

A, 0·0496M-$NH_4I$. B, 0·215M-KI. C, 0·053M-LiI. D, 0·090M-KI. E, 0·053M-KI. F, 0·0492M-NaI. G, 0·048M-HI.

extrapolation to zero iodine concentration are clearly small, and the effect of the added iodine, essential to the operation of the electrode system, can therefore be eliminated and equation (11) used. Extrapolated values of $\left\{\varepsilon_0 + \frac{R}{2F} \ln ([I^-] - [I_2])^3/[I_2]\right\}$ or $P_{\varepsilon,0}$, are shown in Table 1.

TABLE 1.

Values of $P_{\varepsilon,0}$ derived from experimental thermocell data ($\mu$v deg.$^{-1}$). Figures in parentheses have been "corrected" for variations in the ionic activity coefficient terms (see text).

| Salt | Molality | $P_{\varepsilon,0}$ | Salt | Molality | $P_{\varepsilon,0}$ |
|---|---|---|---|---|---|
| $NH_4I$ ..... | 0·0496 | 593 | KI ..... | 0·215 | 563 (521) |
| LiI ..... | 0·053 | 562 | | 0·090 | 556 (522) |
| NaI ..... | 0·0492 | 528 | | 0·053 | 542 (516) |
| HI ..... | 0·048 | 231 | | | |

The variation of $P_{\varepsilon,0}$ with iodide concentration for potassium iodide solutions may be due partly to changes in the term involving the activity coefficient of the iodide ion and its variation with temperature, and partly to changes in the $\sum t_k S^*_k/z_k F$ term. The first

[7] Smith and Eastlack, *J. Amer. Chem. Soc.*, 1916, **38**, 1500.

can be estimated by calculating $\ln f_{\pm} + T \cdot \partial/\partial T \cdot (\ln f_{\pm})$ from a suitable semi-empirical equation such as that suggested by Davies,[8] and the approximate relationship between the activity coefficient and its temperature coefficient derived by Tyrrell and Hollis,[1] writing

$$\log f_{-} = z_{-}/z_{+} \log f_{\pm},$$

a relationship which is consistent with the definition of the mean activity coefficient but not required by it, and ignoring the distinction between the molarity and molality concentration scales. The figures in parentheses in Table 1 (KI only) show values of $[P_{\varepsilon,0} + \boldsymbol{R}(\ln \gamma_{I^-} + T \cdot \partial/\partial T \cdot \ln \gamma_{I^-})]$ obtained in this way. For this salt, the entropy of transfer term is probably almost constant for solutions between 0·053 and 0·215 molal.

In order to apply equation (11) it is necessary to have values of transport numbers, and of the terms involving mean activity coefficients at 30° and a molality of about 0·05. The quantity $(1 + \partial \ln \gamma_{\pm}/\partial \ln m)_{T,P}$ is about 0·97 for all the salts included in Table 1 under these conditions. Cation transport numbers were calculated from the Onsager equation [9]

$$t_{+} = \frac{\lambda^{\circ}_{+} - (\frac{1}{2}|z_{+}|B_2 I^{\frac{1}{2}})/(1 + \kappa a)}{\Lambda^{\circ} - \frac{1}{2}(|z_{+}| + |z_{-}|)B_2 I^{\frac{1}{2}}/(1 + \kappa a)}$$

where $\lambda^{\circ}_{+}$, $\Lambda^{\circ}$ are respectively the equivalent conductance of the cation and of the salt at 30° and at infinite dilution. Also,

$$B_2 = \frac{82{\cdot}5}{\eta(\ni T)^{\frac{1}{2}}}; \quad \kappa a = Ba^{\circ}I^{\frac{1}{2}}$$

where $\eta$ is the viscosity, and $\ni$ the dielectric constant of the solvent. $I$ is the ionic strength, and, at 30°, $B$ has the value 0·3297 for aqueous solutions. This equation gives good agreement with experiment for uni-univalent electrolytes at $I = 0{\cdot}05$. Limiting ionic conductances at 30° were obtained from published data by interpolation,[9] and the ion-size parameters $a^{\circ}$ tabulated by Robinson and Stokes [9] were used, except in the case of ammonium iodide. No data were available for this salt, and a value of 4·15 was selected by comparing the known figures for ammonium chloride with those for the alkali-metal chlorides and iodides. Ammonium iodide was taken as the reference substance, and, if this salt has its Soret coefficient, etc., denoted by the suffix MI, or M, it can be seen from (11) that

$$\sigma_{NI} = \frac{\boldsymbol{F}\Delta P_{\varepsilon,0}}{0{\cdot}97\ (2\boldsymbol{R}Tt_{N})} + \frac{t_M}{t_N} \cdot \sigma_{MI}$$

or

$$\sigma_{NI} = \alpha + \beta\sigma_{MI}$$

where $\alpha$ and $\beta$ are parameters which can be calculated from experimental data on $\Delta P_{\varepsilon,0}$ and transport numbers. These, and the derived values of $\alpha$ and $\beta$ are summarised in Table 2 and compared with some figures derived earlier from measurements on silver–silver iodide electrodes,[1] by using iodide solutions with $I = 0{\cdot}01$.

TABLE 2.

Parameters for the calculation of Soret coefficients.

| Salt | Molality | $\Delta P_{\varepsilon,0}$ ($\mu$v deg.$^{-1}$) | $t_+$ | $10^3\alpha$ (deg.$^{-1}$) | $\beta$ | Data from ref. 1: $10^3\alpha$ (deg.$^{-1}$) | Data from ref. 1: $\beta$ |
|---|---|---|---|---|---|---|---|
| $NH_4I$ | 0·053 | — | 0·490 | — | — | — | — |
| LiI | 0·053 | 31 | 0·324 | 1·9 | 1·51 | 0·8 | 1·5 |
| KI | 0·0496 | 51 | 0·488 | 2·1 | 1·00 | 1·3 | 1·0 |
| NaI | 0·0492 | 65 | 0·389 | 3·4 | 1·26 | 2·5 | 1·2 |
| HI | 0·048 | 362 | 0·823 | 8·9 | 0·60 | — | — |

[8] Davies, *J.*, 1938, 2093.
[9] Robinson and Stokes, "Electrolyte Solutions," Butterworths, London, 2nd edn., 1959.

The values of $\alpha$ and $\beta$ obtained agree roughly with those derived from Preston's measurements [1] on 0·01M-solutions in silver–silver iodide thermocells and should be more accurate. Fig. 3 shows plots of $\sigma_{NI}$ against $\sigma_{MI}$ (MI = $NH_4I$) for sodium, lithium, and potassium iodides derived from these data. Each pair of horizontal lines represents an experimental value for $\sigma_{NI}$, the error in which is assumed to be $\pm 10^{-5}$ deg.$^{-1}$, derived either from Snowdon and Turner's conductimetric measurements [10] at a mean temperature of 25·3° (NaI, KI), or from Alexander's thermogravitational measurements [3] (LiI, NaI, KI: $T_m = 30°$). Both sets of experimental data were obtained for 0·05M-solutions. It can be seen that Snowdon and Turner's values for sodium iodide and potassium iodide in conjunction with the thermocell data lead to almost the same value for $\sigma_{MI}$. A much larger spread in this quantity is obtained if Alexander's values are used to calculate it, in spite of the fact that they were obtained at the same mean temperature as the thermocell data. If it is assumed that the *relative* values of the Soret coefficients of these iodides

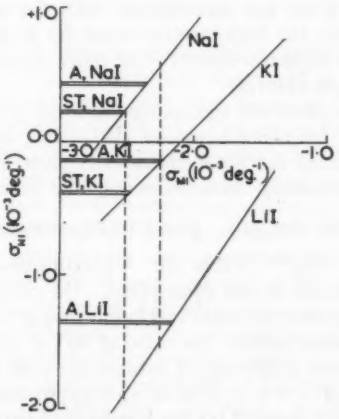


FIG. 3. Graphical test of mutual consistency of thermocell data and Soret coefficient measurements (0·05M-iodide solutions).

A, Alexander's Soret coefficient data [3] at 30°. ST, Snowdon and Turner's Soret coefficient data [10] at 25·3°.

are not much changed between 25° and 30°, the best value for the Soret coefficient of ammonium iodide in 0·05M-solution at 25·3° can be taken to be $-2{\cdot}50 \times 10^{-3}$ deg.$^{-1}$. This is consistent with the conductimetric values for both sodium iodide and potassium iodide, and predicts a Soret coefficient of $-1{\cdot}88 \times 10^{-3}$ deg.$^{-1}$ for 0·05M-lithium iodide at this temperature. No value is available from direct measurements, but, if the difference between the coefficients for sodium and lithium iodide is not very dependent on concentration, Snowdon and Turner's measurements on 0·05M- and 0·01M-solutions lead to a value of about $-1{\cdot}8 \times 10^{-3}$ deg.$^{-1}$ for this solution. Some earlier conductimetric measurements by Agar and Turner [11] gave values for 0·01M-lithium iodide which differed according to whether they were calculated from measurements made during the approach to the steady state or in the steady state itself. Combination of these values with Snowdon and Turner's measurements, with the above assumption, suggests that the value for 0·05M-lithium iodide lies between $-0{\cdot}9$ and $-2{\cdot}2 \times 10^{-3}$ deg.$^{-1}$. In view of the difficulties encountered in the direct measurement of the Soret coefficients of salts with negative Soret coefficients the agreement can be considered good, and, for the limited range of iodides considered here, Snowdon and Turner's measurements fit the thermocell data most satisfactorily.

Table 3 shows Soret coefficients and heats of transfer for 0·05M-iodide solutions at 25° and 30° obtained by using respectively $\sigma_{MI} = -2{\cdot}50 \times 10^{-3}$ and $-2{\cdot}35 \times 10^{-3}$ deg.$^{-1}$ and

[10] Snowdon and Turner, *Trans. Faraday Soc.*, 1960, **56**, 1409.
[11] Agar and Turner, *Proc. Roy. Soc.*, 1960, *A*, **255**, 307.

the parameters shown in Table 2. Heats of transfer have been calculated by assuming that $\left(1 + \frac{\partial \ln \gamma_{\pm}}{\partial \ln m}\right)_{T,P}$ is 0·97 for all salts studied, as before; the error in this is small.

TABLE 3.

Soret coefficients and heats of transfer ($Q_s^*$) for 0·05M-iodide solutions.

| Salt | Soret coefficient ($10^{-3}$ deg.$^{-1}$) | | $Q_s^*$ (cal. mol.$^{-1}$) | |
|---|---|---|---|---|
| | 25° | 30° | 25° | 30° |
| $NH_4I$ | −2·50 | −2·35 | −855 | −822 |
| LiI | −1·88 | −1·50 | −643 | −530 |
| KI | −0·40 | −0·15 | −140 | −50 |
| NaI | +0·24 | +0·56 | +80 | +200 |
| HI | +7·40 | +7·51 | +2530 | +2660 |

Not all of these have been measured directly, but, where this is the case, the values in Table 3 are not inconsistent with the general body of data on Soret coefficients. For example, the high positive value for hydrogen iodide solution is not surprising in view of Tanner's measurements [12] on more concentrated chloride solutions including solutions of hydrogen chloride.

The standard transported entropy of the iodide ion $\bar{S}^{\circ}_{I^-}$ can be calculated, apart from $\Delta S^*_{I^-}$, by using equation (10). $P_{\varepsilon,0}$ and $\sigma$ vary from salt to salt, but the method of calculating the Soret coefficients given in Table 3 ensures that they are consistent with the thermocell measurements, and it is only necessary to carry through the calculation for one salt. For 0·053M-potassium iodide $P_{\varepsilon,0} + \frac{R}{F}(\ln \gamma_{I^-} + T \,.\, \partial/\partial T \,.\, \ln \gamma_{I^-})$ is 516 μV deg.$^{-1}$ (Table 2). Uncertainties in the activity-coefficient term are of minor importance in this connection. On using tabulated [13] values of the standard entropies of the aqueous tri-iodide and iodide ions at 25°, and assuming the difference in these quantities to be substantially the same at 30°, it is found that $\frac{1}{2}(s^{\circ}_{I_3^-} - s^{\circ}_{I^-})$ is 15·48 entropy units. The Soret coefficient of potassium iodide at 30° is, from Table 3, $-0{\cdot}15 \times 10^{-3}$ deg.$^{-1}$, and $2RTt_M(1 + \partial \ln \gamma_{\pm}/\partial \ln m)\,\sigma_M$ is approximately −0·10 entropy unit. When Khoroshin and Temkin's value [14] for the transported entropy of the electron in platinum (4·67 μV deg.$^{-1}$ at 303° K) is included, $(\bar{S}^{\circ}_{I^-} + \Delta S^*_{I^-})$ proves to be 27·4 cal. g.-ion$^{-1}$ deg.$^{-1}$. Haase, Hoch, and Schönert [15] obtained values of 28·1 and 28·4 units, depending on the Soret coefficient values chosen, for $\bar{S}^{\circ}_{I^-}$, using some recent data on silver–silver iodide thermocells, and conductimetric Soret coefficients obtained by Snowdon and Turner and by Agar and Turner. They were able to estimate the variation in the entropy of transfer of the iodide ion with concentration and concluded that it was very small. No such estimate can be obtained from the present data, but the agreement between the transported entropies ($\Delta S^*_{I^-}$ being ignored) is quite good and shows that the two sets of thermocell data are consistent.

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[*Received, June 5th*, 1961.]

[12] Tanner, *Trans. Faraday Soc.*, 1927, **23**, 75.
[13] Latimer, "Oxidation Potentials," Prentice-Hall, New York, 2nd edn., 1959.
[14] Khoroshin and Temkin, *Zhur. fiz. Khim.*, 1952, **26**, 500.
[15] Haase, Hoch, and Schönert, *Z. phys. Chem.* (*Frankfurt*), 1961, **27**, 421.

# 1063. *Fungal Detoxication. Part V.* Metabolism of* o- *and* p-*Chlorophenoxyacetic Acids by* Aspergillus niger.

By J. K. Faulkner and D. Woodcock.

In the metabolism of *p*-chlorophenoxyacetic acid by *Aspergillus niger* (replacement culture technique), 4-chloro-3-hydroxyphenoxyacetic acid, hitherto unknown, is formed in addition to the corresponding 2-hydroxy-acid. When *o*-chlorophenoxyacetic acid is the sole carbon source, hydroxylation takes place at all vacant ring positions, the main products being 2-chloro-4-hydroxyphenoxyacetic acid, together with 2-chloro-5-hydroxyphenoxyacetic acid. The corresponding 3- and 6-hydroxy-compounds are produced in much smaller amounts, and the additional formation of *o*-hydroxyphenoxyacetic acid appears to be the first example of fungal replacement of chlorine by hydroxyl.

Earlier papers in this series [1-3] have shown important differences between the metabolism of aryloxyacetic acids by fungi on the one hand and by micro-organisms and in some cases plants, on the other. In the present paper, the absence of ring fission of *o*- and *p*-chlorophenoxyacetic acid is again a feature of fungal metabolism. This contrasts with the complete breakdown of *p*-chlorophenoxyacetic acid by way of 4-chloro-2-hydroxyphenoxyacetic acid, 4-chlorocatechol, and β-chloromuconic acid, which has been reported by Evans and his co-workers [4,5] using a gram-negative *Pseudomonas*-type soil organism.

Whilst the metabolism of phenoxyacetic acid by *Aspergillus niger* (replacement culture technique) was notable for nuclear hydroxylation without ring fission, substitution being exclusively in *ortho*- and *para*-positions,[2] it has now been shown that with both *p*- and *o*-chlorophenoxyacetic acid hydroxylation takes place at all available positions in the benzene nucleus. Thus the products from the *p*-chloro-acid were, in addition to the expected 2-hydroxy-compound, the hitherto unknown 4-chloro-3-hydroxyphenoxyacetic acid. The latter was identified by an unambiguous synthesis from 4-chloro-3-nitrophenol.

The major metabolic products from *o*-chlorophenoxyacetic acid were 2-chloro-4-hydroxyphenoxyacetic acid and the hitherto unknown 2-chloro-5-hydroxyphenoxyacetic acid, the latter being identical with the compound obtained from 2-chloro-5-ethoxyphenol by successive condensation with ethyl bromoacetate, hydrolysis, and de-ethylation with hydrobromic acid. Two minor metabolities were identified chromatographically as the hitherto unknown 2-chloro-3- and -6-hydroxyphenoxyacetic acid. The former was synthesised from 2-chloro-3-methoxyphenol by a route similar to that used for the 5-hydroxy-acid; 2-chloro-6-hydroxyphenoxyacetic acid was obtained by demethylation of its methyl ether. A fifth acidic compound, which gave a light brown-mauve spot on chromatograms after spraying with *p*-nitrobenzenediazonium fluoroborate, had $R_F$ values indistinguishable from those of *o*-hydroxyphenoxyacetic acid in three solvent systems. Moreover, the infrared absorption spectra were very similar, the absence of the C–Cl peak at 685 cm.$^{-1}$ in the case of the fungal product being significant. This formation of *o*-hydroxy- from *o*-chloro-phenoxyacetic acid appears to be the first example of fungal replacement of chlorine by hydroxyl, though the replacement of carboxyl by hydroxyl is known to occur with *Mycobacterium smegmatis* [6] and with *Penicillium* sp.[7]

* Part IV, Byrde, Downing, and Woodcock, *Biochem. J.*, 1959, **72**, 344.

[1] Byrde, Harris, and Woodcock, *Biochem. J.*, 1956, **64**, 154.
[2] Byrde and Woodcock, *Biochem. J.*, 1957, **65**, 682.
[3] Byrde and Woodcock, *Biochem. J.*, 1958, **69**, 19.
[4] Evans and Smith, *Biochem. J.*, 1958, **57**, xxx.
[5] Evans and Moss, *Biochem. J.*, 1958, **65**, 8P.
[6] Sloane, Crane, and Mayer, *J. Biol. chem.*, 1951, **193**, 453.
[7] Henderson, *J. Gen. Microbiol.*, 1957, **16**, 686.

XUM

## Experimental

Infrared absorption spectra were determined by using a Perkin-Elmer Infracord spectrophotometer.

*Replacement Culture Technique and Detection of Metabolites.*—Cultures of *Aspergillus niger* van Tiegh. (Mulder strain) were grown as previously described.[1] After the medium had been poured from the fungal mat, the under-surface of the latter was washed with water, and a 0·0001M-solution of the acid in 0·01M-disodium hydrogen phosphate introduced underneath it. After incubation for 3 days at 25°, the substrate (6 l.) was strained through muslin and evaporated to 400 ml. under reduced pressure at 40° in a rotary film evaporator. It was then acidified to pH 2 and continuously extracted with ether for 16 hr., the extract washed with water, and acidic material removed by sodium hydrogen carbonate solution. After acidification of the alkaline solution the products were extracted with ether, the extract dried ($Na_2SO_4$), and the solvent removed.

Chromatography was on Whatman no. 1 paper by downward solvent flow, with (A) butanol–ethanol–ammonia (4 : 1 : 5), (B) propanol–ammonia (7 : 3) or (C) benzene–acetic acid–water (3 : 1 : 1) as eluants, system (A) being used for routine examinations. After drying at laboratory temperature chromatograms were sprayed with *p*-nitrobenzenediazonium fluoroborate (1% solution in 20% w/v aqueous sodium acetate) for the detection of phenolic compounds.

*Isolation of Metabolites.*—Separation of small amounts of metabolites was possible by chromatography as a band on Whatman no. 3MM paper, a marker strip being cut and sprayed for location and the required band then extracted with ether saturated with 50% hydrochloric acid. For larger-scale separations partition chromatography with silica gel as supporting medium for the stationary aqueous phase was used. The mobile phase was saturated aqueous chloroform, and approximately 2 ml. fractions were collected automatically.

*Metabolism of* p-*Chlorophenoxyacetic Acid.*—Separation of the acidic material (0·51 g.) obtained from the fungal substrate (30 l.) on a silica column gave unchanged acid (0·39 g.; m. p. and mixed m. p. 156°) and two phenolic acids. The first (0·031 g.), m. p. 127—128°, had $R_F$ 0·43 (solvent A) and was undepressed on admixture with authentic 4-chloro-2-hydroxyphenoxyacetic acid, m. p. 130—131°; the infrared absorption spectra (808, 1180, 1750, 1770 cm.$^{-1}$) were identical. The second acid (0·041 g.) ($R_F$ 0·14) crystallised from aqueous methyl alcohol (10 : 1), m. p. 208° alone or mixed with 4-chloro-3-hydroxyphenoxyacetic acid (Found: C, 47·3; H, 3·7. Calc. for $C_8H_7ClO_4$: C, 47·4; H, 3·5%), $\nu_{max.}$ 685, 833, 1180, 1740, 1760, 3300 cm.$^{-1}$.

*Metabolism of* o-*Chlorophenoxyacetic Acid.*—The acidic material (0·46 g.) from 30 l. of fungal substrate was separated on a silica column and the compounds listed were eluted in the order shown in the Table. 2-Chloro-6-hydroxyphenoxyacetic acid which was obtained mixed with

Metabolism of *o*-chlorophenoxyacetic acid incubated with *A. niger*.

| Subst. in phenoxyacetic acid | Wt. (g.) | $R_F$ in solvent A | B | C | $\nu_{max.}$ (cm.$^{-1}$) | Colour with diazo-reagent | Identification |
|---|---|---|---|---|---|---|---|
| 2-Chloro ..... | 0·25 | — | — | — | 687, 755, 1200, 1750, 1770 | — | Mixed m. p.; I.R. |
| 2-Chloro-6-hydroxy | Trace | 0·66 | 0·75 | — | | Salmon-pink | $R_F$ |
| 2-Hydroxy ..... | 0·008 | 0·45 | 0·60 | 0·19 | 755, 1200, 1750, 1770 | Mauve-brown | $R_F$, I.R. |
| 2-Chloro-3-hydroxy | Trace | 0·13 | 0·31 | — | | Deep pink | $R_F$ |
| 2-Chloro-5-hydroxy | 0·046 * | 0·35 | 0·48 | — | 835, 1185, 1740, 1760, 3300 | Reddish-purple (yellow centre) | Mixed m. p.; I.R. |
| 2-Chloro-4-hydroxy | 0·078 * | 0·35 | 0·50 | — | 805, 1200, 1750, 1770, 3300 | Purple (yellow centre) | Mixed m. p.; I.R. |

* An intermediate mixed fraction of these two acids amounted to 0·07 g.

*o*-chlorophenoxyacetic acid was separated by its greater solubility in cold water. 2-Chloro-5- and -4-hydroxyphenoxyacetic acid, which were inseparable chromatographically on paper in eight solvent systems, were sufficiently separated on the silica column to enable pure specimens to be isolated.

4-*Chloro*-2-*hydroxyphenoxyacetic Acid.*—Prepared as directed by Brown and McCall,[8] this

[8] Brown and McCall, *J.*, 1955, 3681.

compound crystallised from water in needles, m. p. 130—131° (Found: C, 47·4; H, 3·5; Cl, 17·5. Calc. for $C_8H_7ClO_4$: C, 47·5; H, 3·5; Cl, 17·5%) [lit., 124—130° (rapid heating)].

*Ethyl 4-Chloro-3-nitrophenoxyacetate.*—A solution of 4-chloro-3-nitrophenol [9] (4·3 g.) in ethyl alcohol (50 ml.) containing sodium (0·58 g.) was refluxed with ethyl bromoacetate (2·5 ml.) for 0·5 hr., then most of the alcohol was distilled off, the solution was cooled and diluted with water, and the *product* extracted with ether. It crystallised from light petroleum (b. p. 60—80°) in pale yellow rhombic plates (3·8 g.), m. p. 57—58° (Found: C, 46·4; H, 3·8; N, 5·5. $C_{10}H_{10}ClNO_5$ requires C, 46·2; H, 3·85; N, 5·4%). Alkaline hydrolysis gave *4-chloro-3-nitrophenoxyacetic acid*, yellow felted needles (from aqueous methyl alcohol), m. p. 137—137·5° (Found: C, 41·7; H, 2·4; N, 6·0. $C_8H_6ClNO_5$ requires C, 41·5; H, 2·6; N, 6·0%).

*Ethyl 3-Amino-4-chlorophenoxyacetate.*—A solution of the above nitro-ester (2 g.) in tetrahydrofuran (20 ml.) was shaken in hydrogen in the presence of Raney nickel until further uptake of gas ceased (671 ml.). After removal of catalyst and solvent the product was distilled *in vacuo*. The *ester* crystallised from benzene–light petroleum (b. p. 40—60°) in stout prisms, m. p. 62—63° (Found: C, 52·6; H, 5·4. $C_{10}H_{12}ClNO_3$ requires C, 52·3; H, 5·2%). Alkaline hydrolysis followed by benzoylation gave *3-benzamido-4-chlorophenoxyacetic acid*, monoclinic prisms (from aqueous methyl alcohol), m. p. 172—173° (Found: C, 59·0; H, 4·0. $C_{15}H_{12}ClNO_4$ requires C, 58·9; H, 3·9%).

*4-Chloro-3-hydroxyphenoxyacetic Acid.*—A suspension of the above amino-ester (0·46 g.) in 10% sulphuric acid (10 ml.) was stirred during dropwise addition of sodium nitrite (0·15 g.) in water (2 ml.). The filtered solution was decomposed by gradual addition to a boiling solution of copper sulphate pentahydrate (10 g.) in water (10 ml.), the solution being then cooled and extracted with ether. The acidic *product* was set free from 10% aqueous sodium hydroxide by acidification and extracted with ether. The ethereal solution was dried ($Na_2SO_4$), the solvent removed, and the residue crystallised from aqueous methyl alcohol (10 : 1) (charcoal). It had m. p. 207—208° (Found: C, 47·4; H, 3·6. $C_8H_7ClO_4$ requires C, 47·4; H, 3·5%).

*2-Chloro-5-ethoxyphenol.*—A solution of 2-chloro-5-ethoxyaniline [10] (5·8 g.) in water (27 ml.) and sulphuric acid (3 ml.) was stirred at 0° during dropwise addition of sodium nitrite (2·3 g.) in water (6 ml.). After being stirred for a further 0·25 hr. the solution was filtered and the filtrate gradually added to copper sulphate pentahydrate (50 g.) in boiling water (50 ml.), and the product was continuously steam-distilled off. Extraction of the distillate with ether gave 2-chloro-5-ethoxyphenol (2·2 g.), b. p. 230°/762 mm. It formed a *3,5-dinitrobenzoate*, m. p. 152—152·5° (from aqueous methyl alcohol) (Found: C, 49·4; H, 3·2; N, 7·5. $C_{15}H_{11}ClN_2O_7$ requires C, 49·1; H, 3·0; N, 7·6%), and a *phenylurethane*, m. p. 125—126° [from light petroleum (b. p. 100°)] (Found: C, 61·4; H, 4·6; N, 5·2; Cl, 11·7. $C_{15}H_{14}ClNO_3$ requires C, 61·8; H, 4·8; N, 4·8; Cl, 12·2%).

*2-Chloro-5-ethoxyphenoxyacetic Acid.*—This was prepared from 2-chloro-5-ethoxyphenol (0·9 g.) and ethyl bromoacetate. The *product* (1·1 g.) crystallised from aqueous methyl alcohol in rhombic prisms, m. p. 145—146° (Found: C, 52·3; H, 4·7; Cl, 15·4.. $C_{10}H_{11}ClO_4$ requires C, 52·1; H, 4·8; Cl, 15·4%).

*2-Chloro-5-hydroxyphenoxyacetic Acid.*—The above 5-ethoxy-compound (0·85 g.) was refluxed with hydrobromic acid (*d* 1·48; 10 ml.) for 1 hr. and then the solution was cooled, diluted with water, and extracted with ether. The acidic *product* (0·73 g.) obtained by washing the extract with sodium hydrogen carbonate solution, acidification, and re-extraction, crystallised from water in needles, m. p. 135—136° (Found: C, 45·5, 45·8; H, 3·6, 3·7; Cl, 17·2, 17·3%; equiv., 212. $C_8H_7ClO_4,\frac{1}{2}H_2O$ requires C, 45·45; H, 3·8; Cl, 16·8%; equiv., 211·5). The ethyl ether, prepared by using diethyl sulphate, crystallised from aqueous methyl alcohol in rhombic prisms, m. p. 146—147°, undepressed on admixture with the ethoxy-acid prepared earlier.

*2-Chloro-3-methoxyphenol.*—This was prepared in 20% yield from 2-chloro-3-methoxyaniline [9] by the method used for 2-chloro-5-ethoxyphenol. It had b. p. 227—228°/762 mm., m. p. (prisms) 56—58° (Found: C, 53·1; H, 4·4. $C_7H_7ClO_2$ requires C, 53·0; H, 4·4%). The *3,5-dinitrobenzoate* crystallised from aqueous methyl alcohol in pale yellow prisms, m. p. 148° (Found: C, 47·5; H, 2·9; N, 8·1. $C_{14}H_9ClN_2O_7$ requires C, 47·7; H, 2·6; N, 7·95%).

*2-Chloro-3-methoxyphenoxyacetic Acid.*—This *acid* was prepared from the corresponding phenol by condensation with ethyl bromoacetate. It crystallised from aqueous methyl alcohol in plates, m. p. 188—189° (Found: C, 49·9; H, 4·1. $C_9H_9ClO_4$ requires C, 49·9; H, 4·2%).

[9] Clemo and Daglish, *J.*, 1950, 1481.
[10] Van Erp, *J. prakt. Chim.*, 1930, **127**, 31.

*2-Chloro-3-hydroxyphenoxyacetic Acid.*—2-Chloro-3-methoxyphenoxyacetic acid (0·4 g.) was demethylated by refluxing it with hydrobromic acid (*d* 1·48; 10 ml.) for 1 hr. The *product* (0·3 g.) crystallised from water in prisms, m. p. 176—177·5° (Found: C, 47·9; H, 3·6; Cl, 17·7. $C_8H_7ClO_4$ requires C, 47·7; H, 3·5; Cl, 17·5%).

*Ethyl 2-Chloro-3-nitrophenoxyacetate.*—Prepared from 2-chloro-3-nitrophenol [10] (1·75 g.) by condensation with ethyl bromoacetate, the *product* (1·9 g.) crystallised from aqueous methyl alcohol in monoclinic prisms, m. p. 82—83° (Found: C, 46·5; H, 4·0; N, 5·5. $C_{10}H_{10}ClNO_5$ requires C, 46·2; H, 3·85; N, 5·4%). Alkaline hydrolysis gave the corresponding *acid*, m. p. 177—178° (from aqueous ethyl alcohol) (Found: C, 41·7; H, 2·5; N, 6·0. $C_8H_6ClNO_5$ requires C, 41·5; H, 2·6; N, 6·0%).

*2-Chloro-6-methoxyphenoxyacetic Acid.*—A solution of 3-chloroguaiacol [9] (1·6 g.) in ethyl alcohol (20 ml.) containing sodium (0·23 g.) was refluxed for 4 hr. with ethyl bromoacetate (1·7 g.). After the addition of 10% sodium hydroxide (20 ml.) and refluxing for a further 0·5 hr. the solution was cooled, acidified, and extracted with ether. The required acid (1·6 g.) crystallised from benzene–light petroleum (b. p. 40—60°) in prisms, m. p. 120—121° (Found: C, 49·3; H, 3·9. Calc. for $C_9H_9ClO_4$: C, 49·9; H, 4·2%). Brown and McCall state in a personal communication that their m. p. 130° is an error.

*2-Chloro-6-hydroxyphenoxyacetic Acid.*—The above methoxy-acid (1·04 g.) was refluxed with hydrobromic acid (*d* 1·48; 10 ml.) for 1 hr. The solution was cooled, diluted with water, and extracted with ether. After being washed with water, the extract was dried ($Na_2SO_4$) and the solvent removed. The *product* crystallised from light petroleum (b. p. 40—60°) in prisms, m. p. 98—99° (Found: C, 47·3; H, 3·2; Cl, 17·4. $C_8H_7ClO_4$ requires C, 47·4; H, 3·5; Cl, 17·5%). Refluxing this with acetic anhydride for 1 hr. gave *5-chloro-2-oxo-1,4-benzodioxan*, m. p. 46—48°, purified by sublimation *in vacuo* (Found: C, 51·7; H, 2·4. $C_8H_5ClO_3$ requires C, 52·0; H, 2·7%).

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## 1064. *Indicine: the Major Alkaloid of* Heliotropium indicum *L.*

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*Heliotropium indicum* from Ghana and from Australia contains a new pyrrolizidine alkaloid, indicine (I), and its *N*-oxide, with minor unidentified alkaloids.

In a study of potentially hepatotoxic plants, *Heliotropium indicum* was of interest as it is one of the most widely used herbs in the Ayurvedic medicine of India [1] and in some other countries in which liver diseases are common.[2] Pyrrolizidine alkaloids have previously been isolated from *Heliotropium lasiocarpum* (heliotrine, lasiocarpine),[3] *H. europaeum* (heliotrine, lasiocarpine, supinine, europine),[4] and *H. supinum* (supinine, echinatine).[5] All of these have proved to be hepatotoxic.[6]

[1] Kirtikar, Basu, and An, "Indian Medicinal Plants," Allahabad, 2nd edn., 1936, Vol. III, p. 1689; Nadkarni, "Indian Materia Medica," Nadkarni, Bombay, 1927, p. 422.

[2] Dalziel, "The Useful Plants of West Tropical Africa," Crown Agents for the Colonies, London, 1937, p. 725; Dragendorff, "Die Heilpflanzen der verschiedenen Völker und Zeiten," F. Enke, Stuttgart, 1898.

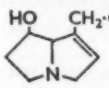
[3] Menshikov, *Ber.*, 1932, **65**, 974.

[4] Culvenor, Drummond, and Price, *Austral. J. Chem.*, 1954, **7**, 277; Culvenor, *ibid.*, p. 287.

[5] (*a*) Menshikov and Gurevich, *Zhur. obshchei Khim.*, 1949, **19**, 1382; (*b*) Crawley and Culvenor, *Austral. J. Chem.*, 1959, **12**, 694.

[6] Bull, Dick, and McKenzie, *J. Path. Bact.*, 1958, **75**, 17; Bull and Dick, *ibid.*, 1959, **78**, 483, and unpublished results; Schoental and Magee, *ibid.*, 1957, **74**, 305; 1959, **78**, 471.

Independent studies in England and in Australia (where *H. indicum* is naturalised and a potential danger to stock) have led to identification of the major alkaloid, indicine (I), as the (−)-trachelanthic ester of retronecine. Results from the two laboratories are here presented jointly.



(I)

In plant material from Ghana and from Australia, the alkaloid occurred largely as the *N*-oxide, with considerable variation in total alkaloid content. Isolation of the crude alkaloid was greatly facilitated by the use of cation exchange-resin,[7] which retained both the alkaloids and their *N*-oxides. After reduction of oxides, the crude base consisted of one major component, indicine, with small amounts of minor alkaloids. Best isolated by means of its picrate or picrolonate, indicine had the empirical formula $C_{15}H_{25}NO_5$.

Alkaline hydrolysis of indicine gave retronecine and an acid $C_7H_{14}O_4$ whose properties closely resembled those of trachelanthic acid in all except sign of specific rotation. Periodate oxidation of the acid gave acetaldehyde, isobutyric acid, and carbon dioxide, showing that it is an αβ-dihydroxy-α-isopropylbutyric acid. It was identified as the enantiomeric (−)-form of trachelanthic acid by formation of the racemate with the (+)-form obtained by hydrolysis of supinine, and by the identity of the infrared spectrum of the enantiomers. Evidence that the acid esterifies the primary hydroxyl group of retronecine was obtained by catalytic hydrogenolysis of indicine to (−)-trachelanthic acid and retronecanol.

Indicine is the first alkaloid from a *Heliotropium* species to contain retronecine as the basic moiety; the isomeric heliotridine has hitherto been found in this genus. However, esters of retronecine with monocarboxylic acids have been found in other genera of the *Boraginaceae*, namely, *Echium*, *Cynoglossum*, and *Amsinckia*.[8] (−)-Trachelanthic acid is the third isomer of αβ-dihydroxy-α-isopropylbutyric acid to occur as an esterifying acid in pyrrolizidine alkaloids. (+)-Trachelanthic acid and (−)-viridifloric acids have previously been found in several alkaloids of the *Boraginaceae*.[9,5b]

Several derivatives of indicine including the *N*-oxide, which is deliquescent, have been prepared. The picrate forms solvates with properties suggesting that they are clathrate compounds.[10]

Paper chromatography of the alkaloids in butanol–acetic acid gave more compact spots and more reproducible $R_F$ values on paper buffered with sodium acetate.[11] *E.g.*, $R_F$ values of indicine on unbuffered paper ranged from 0·32 to 0·39, according to the quantity spotted; on buffered paper they varied only from 0·56 to 0·58.

## Experimental

*Paper Chromatography of Alkaloids.*—Except where otherwise stated, descending chromatograms were run on Whatman no. 1 paper, buffered with 0·1M-sodium acetate,[11] with butan-1-ol–acetic acid–water as solvent.[5b] Spots were detected by exposing the dried paper to iodine vapour.

*Isolation of Alkaloids from* Heliotropium indicum.—(a) *From Ghana.* Dried ground plant (2·04 kg.) was continuously percolated for 9 hr. with ethanol at room temperature, a column of Dowex 50 resin (200—400 mesh; acid form; 100 g. damp) being included in the circuit.[7] The Dowex column was washed with ethanol and with water, and the bases were eluted with ~0·8N-aqueous ammonia (300 ml.). The eluate was reduced with sulphuric acid and zinc dust to convert *N*-oxides into bases, and extracted from alkaline solution with chloroform, to give a pale brown gum (8 g.). Paper chromatography showed a large spot, $R_F$ 0·58 (indicine), and weak spots, $R_F$ 0·26 (retronecine) and 0·69 (unidentified alkaloid).

When the plant (11 kg.) was twice soaked in ethanol (total 20 l.), and the extract passed through a column of Dowex 50, the crude alkaloids, obtained as described above, formed an

[7] Mattocks, *Nature* 1961, **191**, 1281.
[8] Culvenor, *Austral. J. Chem.*, 1956, **9**, 512, and unpublished results.
[9] Leonard, "The Alkaloids," ed. Manske, Academic Press, 1960, Vol. VI, p. 35.
[10] Powell, *J.*, 1948, 61.
[11] Munier, Macheboeuf, and Cherrier, *Bull. Soc. Chim. biol.*, 1952, **34**, 204.

almost colourless gum (15·6 g.). This partly crystallised during several weeks at room temperature. Recrystallisation from light petroleum (b. p. 80—100°) or from benzene–hexane gave colourless hexagonal prisms of *indicine*, m. p. 97—98°, $[\alpha]_D^{20}$ +22·3° (*c* 1·65 in EtOH), $R_F$ 0·58 (Found: C, 60·1; H, 8·3; N, 5·0. $C_{15}H_{25}NO_5$ requires C, 60·2; H, 8·3; N, 4·7%). On a larger scale this alkaloid was best recrystallised from diethyl ether.

By chromatography on a column of Hyfio Supercel (140 g., depth 43 cm.) buffered with M/15-disodium hydrogen phosphate (70 ml.) and elution with various chloroform–carbon tetrachloride mixtures, the crude reduced material (3 g.) yielded pure indicine (1·4 g.; $R_F$ 0·58 only) and a mixture of indicine with the substance, $R_F$ 0·69.

By chloroform extraction of aqueous extracts before and after reduction, two batches of *H. indicum* from Ghana were found to contain tertiary base, 0·009%, *N*-oxide 0·08%, and base, 0·045%, *N*-oxide 0·345%, respectively.

(b) *From Australia.* Preliminary assay [12] showed that the plant contained 0·23% of tertiary base and 0·18% of *N*-oxide (2 earlier samples from different parts of Queensland contained base 0·09%, oxide 0·37%, and base 0·09%, oxide 1·33%, respectively). A hot methanol extract of dried plant tops (10 lb.) was evaporated and the residue extracted with dilute sulphuric acid. Reduction and extraction with chloroform gave the crude alkaloid as a gum (24 g.), apparently nearly all one base ($R_F$ 0·34 on unbuffered paper with ascending chromatography). A portion of this gum (8 g.) was treated with a slight excess of picrolonic acid in ethanol, the solution evaporated, and the residue extracted with hot water. *Indicine picrolonate* (9·5 g.), m. p. 108—109°, crystallised on cooling. Recrystallisation from aqueous ethanol gave crystals, m. p. 108—109°. The m. p. was raised to 115—117° by drying for 3 hr. at 100° but the picrolonate still contained water of crystallisation (Found: C, 52·0; H, 6·0; N, 12·1. $C_{15}H_{25}NO_5,C_{10}H_8N_4O_5,H_2O$ requires C, 51·6; H, 6·0; N, 12·0%). Base, recovered from the picrolonate by means of Deacidite FF resin, was a gum.

*Indicine Salts.*—Pure indicine, in ethanol, was neutralised with ethanolic hydrogen chloride, excess of dry ether was added, and the product was recrystallised from ethanol–ether to give hygroscopic, rectangular leaflets of the *hydrochloride*, m. p. 131—132°, $[\alpha]_D^{20}$ +11·25° (*c* 4·54 in EtOH) (Found: C, 53·9; H, 7·9; N, 4·4; Cl, 10·9. $C_{15}H_{25}NO_5,HCl$ requires C, 53·6; H, 7·8; N, 4·2; Cl, 10·6%).

Aqueous indicine hydrochloride, treated with saturated ammonium reineckate solution, yielded the *reineckate*, pale pink blades (from water), m. p. 141—142° {Found: C, 36·8; H, 5·6. $C_{15}H_{26}NO_5[Cr(NH_3)_2(SCN)_4]$ requires C, 36·9; H, 5·2%}.

Indicine (0·3 g.) in benzene was neutralised with picric acid; the *picrate* (0·5 g.), after several recrystallisations from benzene formed leaflets, m. p. 88—90° (efferv.). The recrystallised picrate was redissolved in hot benzene, and portions of the solution were cooled, (*a*) very slowly, giving leaflets, m. p. 90° (efferv.) (Found: C, 53·4; H, 5·3; N, 9·5. $C_{15}H_{25}NO_5,C_6H_3N_3O_7,C_6H_6$ requires C, 53·5; H, 5·6; N, 9·2%), and (*b*) rapidly, giving leaflets, m. p. 81—86° (efferv. above 90°) (Found: C, 51·0; H, 5·5; N, 10·3. $C_{15}H_{25}NO_5,C_6H_3N_3O_7,0{\cdot}62C_6H_6$ requires C, 51·3; H, 5·5; N, 9·7%).

The slowly recrystallised picrate (68·3 mg.) was dried *in vacuo* for 3 days at room temperature over $P_2O_5$, KOH, and paraffin wax, without loss in weight. It was then heated *in vacuo* during 8 min. from 60° to 90°, and then to 100°. Vigorous effervescence occurred at first, but ceased completely after ½ hr. at 100°. The volatile product was collected in a cold trap, and diluted with hexane; benzene (8·0 mg.) was identified and estimated by its ultraviolet spectrum.[13] The loss in weight was 8·1 mg. (11·9%. Calc. for 1 mol. of benzene of crystallisation: 12·9%).

In a similar experiment the rapidly recrystallised picrate lost 6·1% by wt.

The glassy residue, recrystallised twice from water, gave a *hydrate* as platelets, m. p. 66—68°, without effervescence up to 140° (Found: C, 46·6; H, 5·4; N, 10·5. $C_{15}H_{25}NO_5,C_6H_3N_3O_7,H_2O$ requires C, 46·2; H, 5·5; N, 10·3%).

Samples of indicine, recovered from the picrate before and after heating, had identical $R_F$ values (0·58).

Indicine (0·2 g.) in chloroform was treated with methyl iodide for 5 min. at room temperature, the solvent removed, and the residue recrystallised from ethanol–ether to give the *methiodide* as blades (0·21 g.), m. p. 159—160°, $[\alpha]_D^{20}$ +12·5° (*c* 4·32 in EtOH) (Found: C, 44·4; H, 6·15; N, 3·2; I, 29·4. $C_{16}H_{28}INO_5$ requires C, 43·5; H, 6·35; N, 3·2; I, 28·8%).

[12] Culvenor and Smith, *Austral. J. Chem.*, 1955, **8**, 556.
[13] Tunnicliff, Brattain, and Zumwalt, *Analyt. Chem.*, 1949, **21**, 890.

When the methiodide was hydrolysed with dilute alkali, an acid was obtained, m. p. 86°, not depressed by the acid obtained by hydrolysing indicine.

*Indicine* N-*Oxide*.—Indicine (0·5 g.) in ethanol (4 ml.) was treated with 30% hydrogen peroxide (2 ml.) for 3 days at room temperature. The excess of reagent was destroyed with manganese dioxide, and the filtered solution was evaporated under reduced pressure. The deliquescent residue was dissolved in a little methanol, reprecipitated with acetone and ether, cooled, and rubbed to induce crystallisation. Recrystallisation from methanol–acetone gave colourless, deliquescent needles, which were isolated by centrifugation and washing with ether and light petroleum (b. p. 30—40°) in the centrifuge tube, and were dried by slow evacuation in a desiccator over $P_2O_5$. The solvated *N*-oxide had m. p. 130—131° (decomp. 165—166°), $[\alpha]_D^{20}$ +34·0° (*c* 7·0 in EtOH) (Found: C, 56·1; H, 8·25; N, 3·75. Calc. for $C_{15}H_{25}NO_6$: C, 57·1; H, 7·9; N, 4·4. Calc. for $C_{15}H_{25}NO_6,CH_3{\cdot}OH$: C, 55·3; H, 8·35; N, 4·0%).

*Hydrolysis of Indicine*.—Indicine (1·2 g.) was heated in 2N-sodium hydroxide at 100° for 2 hr., and the solution was acidified and extracted with ether to give an acid (0·55 g.) which crystallised from benzene–light petroleum in rosettes, m. p. 94°, $[\alpha]_D$ −3·4° (Found: C, 51·9; H, 8·7. Calc. for $C_7H_{14}O_4$: C, 51·8; H, 8·7%). A mixture of equal quantities of this acid with (+)-trachelanthic acid, after melting and cooling, remelted at 118—119° (racemic trachelanthic acid has m. p. 119—121° [14]). The *brucine salt* of the acid from indicine formed needles (from ethanol), m. p. 197—198° (Found: C, 63·1; H, 7·2; N, 4·9. $C_7H_{14}O_4,C_{23}H_{26}N_2O_4$ requires C, 63·7; H, 7·2; N, 5·0%). Adams and van Duuren [14] and Dry and Warren [14] record 183—187° and 196—198°, respectively, for the m. p. of the brucine salt of synthetic (−)-trachelanthic acid.

The basic product of hydrolysis was isolated by neutralising the solution from which acid has been extracted, evaporating it to dryness, extracting the residue with ethanol, and passing the extract, diluted with an equal volume of water, through Deacidite FF resin. Evaporation of the eluate gave a base (0·55 g.) ($R_F$ 0·26) which crystallised from acetone in prisms, m. p. 118—119°, undepressed on admixture with retronecine (Found: C, 62·1; H, 8·5; N, 9·2. Calc. for $C_8H_{13}NO_2$: C, 62·0; H, 8·4; N, 9·0%).

*Oxidation of the Acid from Hydrolysed Indicine*.—(*a*) The acid (62·3 mg.), oxidised with 0·5M-sodium metaperiodate [15] (2 ml.) at room temperature for 30 min., absorbed 1·91 mol. of periodate. After an additional 1 hour's heating at 80—90°, the total periodate absorbed was 1·95 mol.

(*b*) The acid (115 mg.) was oxidised as above, the solution was flushed with nitrogen, and this was passed in turn through 2,4-dinitrophenylhydrazine reagent and barium hydroxide solution. This gave much barium carbonate and the acetaldehyde 2,4-dinitrophenylhydrazone (45 mg.), m. p. and mixed m. p. 151—152°.

The oxidation mother liquor, when saturated with calcium chloride and extracted with ether, yielded a pungent acid whose anilide formed colourless leaflets (from water), m. p. 103—104° alone or mixed with isobutyranilide.

*Hydrogenolysis of Indicine*.—In dilute hydrochloric acid, in the presence of platinum oxide, indicine absorbed 2 mol. of hydrogen. Filtration and extraction with ether gave (−)-trachelanthic acid, m. p. 94° (from benzene–light petroleum), identical with the acid obtained by hydrolysis. The residual aqueous solution was made alkaline and extracted with chloroform to give retronecanol, crystallising from light petroleum in prisms, m. p. and mixed m. p. 92— 93° (Found: C, 68·1; H, 10·6; N, 10·3. Calc. for $C_8H_{15}NO$: C, 68·1; H, 10·6; N, 9·9%). It formed a picrate, m. p. 211—213°, from ethanol, undepressed on admixture with retronecanol picrate.[16]

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[14] Adams and Van Duuren, *J. Amer. Chem. Soc.*, 1952, **74**, 5349; Dry and Warren, *J.*, 1952, 3445.
[15] Christie, Kropman, Novellie, and Warren, *J.*, 1949, 1703.
[16] Barger, Seshadri, Watt, and Yabuta, *J.*, 1935, 11; Adams and Rogers, *J. Amer. Chem. Soc.*, 1939, **61**, 2815.

XUM

## 1065. *Acylation. Part II.* Friedel–Crafts Acylation, with Stannic Chloride as Catalyst, in Solvents of Low Dielectric Constant.*

By D. P. N. Satchell.

At 25°, in carbon tetrachloride, with stannic chloride as catalyst, β-naphthol, *p*-methoxyphenol, and *m*-nitrophenol are acylated by both aromatic and aliphatic acid chlorides at the hydroxylic oxygen atom to give esters, rather than in the ring to give ketones. In ethylene dichloride some nuclear attack may occur, though the predominant product remains the ester.

Kinetic experiments with either carbon tetrachloride or ethylene dichloride as solvent show an order of unity for the phenol, one of close to unity for stannic chloride, and an order variable from unity to *ca.* 1·7 for the acid chloride, whether aliphatic or aromatic. The products do not appreciably retard the reaction.

The effect of changes in dielectric constant and in solvent structure have also been examined. Co-ordinating additives either increase or decrease the reaction rate according to their concentration.

The essential differences from the behaviour with aluminium chloride as catalyst are discussed, and the likely mechanisms for catalysis by stannic chloride and aluminium chloride are compared. It is shown that, with stannic chloride, intermediate complexes containing two mol. of acid chloride are involved as well as those containing only one. With stannic chloride, acetyl chloride is a more reactive acylating agent than benzoyl chloride, and within both the aliphatic and aromatic series electron-repelling substituents in the acid halide facilitate reaction, and electron-withdrawing substituents retard it. Similar effects are not necessarily to be expected for catalysis by aluminium chloride.

There has been little advance in the understanding of Friedel–Crafts acylation by acid chlorides since the first quarter of the century. By then it was realised [1] (*a*) that alkylated benzenes were attacked more readily than benzene itself, *i.e.*, that the reaction involved what is now termed an electrophilic substitution, (*b*) that complexes of some kind between the catalyst and acylating agent were involved, and (*c*) that reaction was often retarded by complex formation between the catalyst and the products. The two main advances since that time might be considered to be (1) the explicit realisation [2] that the reaction is really diverse in its manifestations and that no single mechanism is likely to embrace them all, and (2) a kinetic study of, among other things, the effects of different catalysts, which clearly illustrates this very point. In this study [3] the catalytic effects of different Lewis acids were revealed as subtly related to their co-ordinating powers.

In view of the specificity of the mechanistic detail to particular sets of reagents there are inevitably several aspects of the reaction which remain largely unclarified. These are: (i) The effect on reactivity of changing the halide in the acyl halide along the series F, Cl, Br, I. (The generality of the Calloway series [4] is now in doubt.[5] To mention one point only, it seems obvious that the stereochemical requirements of the particular catalyst will influence the order.) (ii) The nature of the active complex between acylating agent and catalyst. (It seems clear that both oxonium and acyl cation complexes will be formed in many cases. Whether or not the oxonium species can lead to significant acylation is

* *J.*, 1960, 1752, is considered as Part I.

[1] Steele, *J.*, 1903, **83**, 1470; Perrier, *Ber.*, 1900, **33**, 815; Boeseken, *Rec. Trav. chim.*, 1901, **20**, 102; Meerwien, *Annalen*, 1927, **455**, 227; Olivier, *Rec. Trav. chim.*, 1914, **33**, 244.

[2] Burton and Praill, *Chem. and Ind.*, 1954, 90.

[3] Jensen and Brown, *J. Amer. Chem. Soc.*, 1958, **80**, 2291, 3039; see also Ahmad, Baddeley, and Topping, *Chem. and Ind.*, 1958, 1327.

[4] Calloway, *J. Amer. Chem. Soc.*, 1937, **59**, 1474.

[5] Yamase and Goto, *J. Chem. Soc. Japan*, 1960, **81**, 1906.

not definitely decided.[3,6]) (iii) The effect on reactivity of changes in structure in the acyl group. (The few available data [6,7] do not permit any decision.) (iv) The effect of changes of solvent. (Complex effects are observed [8] and this topic promises to be most involved.) (v) The effect of a change in catalyst.

Jensen and Brown's systematic kinetic work [3] is an important start on the last subject, and indeed kinetic studies provide the main hope of resolving all the above problems. So far, however, such studies have been few, and recent papers by Brown and his colleagues [9] essentially confirm and considerably augment previous kinetic investigations. The earlier work [10] was largely concerned with catalysis by aluminium chloride in solvents of low polarity. Brown and his colleagues have also examined catalysis by aluminium chloride in nitrobenzene [8a] and catalysis by various Lewis acids [3] in benzoyl chloride as solvent-reactant. As noted, significant differences were observed for the different types of system. These are discussed below in so far as they relate to the results of the present study which concerns catalysis by stannic chloride in solvents of low polarity. The effect on the reaction of structural changes in the acid halide has been examined.

The reactions to be described are somewhat unusual in that, while previous kinetic investigations all involved the nuclear acylation of an aromatic compound to give a ketone, the present work involves acylation of phenolic compounds under conditions where acylation of the hydroxyl group predominates over ketone formation.

## Experimental

*Materials.*—" AnalaR " carbon tetrachloride was refluxed over phosphorus pentoxide, and reagent-grade ethylene dichloride over calcium hydride for several hours, before fractional distillation; they had b. p. 76° and 83·4°, respectively. Dry acetic acid was prepared as previously described.[11] Ether was refluxed over sodium and then fractionally distilled (b. p. 34—35°). Stannic chloride and titanic chloride were purified by a method described previously.[12] Germanium tetrachloride (Johnson Matthey) was used without purification. Acetyl, propionyl, and n-butyryl chloride were refluxed over isoquinoline (to remove free acid), then fractionally distilled; they had b. p. 51°, 79°, and 102—103° respectively. Samples of acetyl chloride purified by use of dimethylaniline rather than isoquinoline gave essentially identical kinetics. Chloroacetyl chloride was fractionated and a sample of b. p. 105° collected. Benzoyl and *p*-toluoyl chloride were also fractionally distilled; they had b. p. 197° and 220°, respectively. β-Naphthol, *m*-nitrophenol, and *p*-methoxyphenol were recrystallised samples of m. p. 122°, 97°, and 56°, respectively. Standard samples of β-naphthyl acetate, propionate, butyrate, and benzoate, *m*-nitrophenyl acetate, and *p*-methoxyphenyl acetate, prepared by Vogel's method,[13] had m. p. 69°, m. p. 51°, b. p. 122°/0·5 mm., m. p. 106°, 53°, and 31° respectively.

*Reaction Mixtures.*—Contamination of reagents and reaction mixtures by atmospheric moisture was kept at a low level. The dried reagents (see above) were stored in a dry box, where the reaction mixtures were also made up. This procedure especially facilitates the handling of stannic and titanic chloride.

The reaction mixtures were made up in 10 (or 25) ml. volumetric flasks with ground-glass stoppers. When β-naphthol and *p*-methoxyphenol were being acylated these compounds were added as solids: they dissolved in the solvents involved fairly rapidly. *m*-Nitrophenol dissolves rather slowly and was therefore added as a solution in the appropriate solvent. All other components were also added as measured volumes, sometimes (*e.g.*, for stannic chloride) as volumes of stock solutions in the appropriate solvent.

*Kinetic Arrangements.*—The stoppered reaction flasks were removed from the dry box and

[6] (*a*) Jensen, Marino, and Brown, *J. Amer. Chem. Soc.*, 1959, **81**, 3303; (*b*) Brown, Marino, and Stock, *ibid.*, p. 3310; (*c*) Jensen, *ibid.*, 1957, **89**, 1226.
[7] Cullinane, Chard, and Leyston, *J.*, 1952, 376; Man and Hauser, *J. Org. Chem.*, 1952, **17**, 397.
[8] (*a*) Brown and Young, *J. Org. Chem.*, 1957, **22**, 719; (*b*) Gore, *Chem. Rev.*, 1955, **55**, 229.
[9] Refs. 3, 6, and 8, and associated papers.
[10] Ref. 6(*a*) contains a summary of previous work.
[11] Satchell, *J.*, 1956, 3911.
[12] Satchell, *J.* 1960, 4388.
[13] Vogel, " Practical Organic Chemistry," Longmans, Green and Co., London, 1948.

additionally sealed with Apiezon Q compound to help exclude atmospheric moisture. They were then kept at 25° by partial immersion in a thermostat bath. At intervals 1 (or 2) ml. samples were quickly withdrawn and run into sufficient glacial acetic acid effectively to stop the reaction. The resulting solution was made up to 25 ml. The extent of acylation was followed by measurements of the intensity of the light absorption at 3300 Å (3000 Å for *p*-methoxyphenol) where absorption due to the unacylated phenol predominates.[14] (For *m*-nitrophenol allowance was made for the small but significant absorption of the ester produced.) There was no interference from the other reaction components. Spectral measurements were made with a Unicam S.P. 500 spectrophotometer.

The concentration of phenol in the reaction mixtures was usually *ca.* $5 \times 10^{-3}$M though for some experiments it was reduced to *ca.* $2{\cdot}5 \times 10^{-3}$M. The acid chloride was kept in at least *ca.* 10-fold excess over the phenol, a procedure which helped to simplify the kinetic behaviour. Except for acylation in ethylene dichloride (see below) good first-order plots for the loss of phenol were obtained. Reproducibility with different samples of reagents and on different occasions was satisfactory.

*Stoicheiometry of Reactions.*—Indepedent preparative-scale experiments were conducted for most of the reactions studied kinetically. These preparations were carried out at concentrations and temperatures similar to those obtaining in the kinetic experiments.

## Results and Discussion

*Reaction Products*: *Oxygen* versus *Nuclear Acylation.*—Phenolic compounds may be acylated at the hydroxyl group or at an aromatic carbon atom, or both. Previous evidence,[15] which chiefly concerns catalysis by aluminium chloride, indicates the effect of the solvent. Use of solvents of high polarity, such as nitrobenzene, usually results in nuclear acylation only, probably because the phenolic oxygen atom is largely engaged by the catalyst and so protected. With solvents of low dielectric constant we may presume that engagement is less complete and that reaction can result in a mixture in which the ester may even predominate. This appears the case, for example, for the reactions of phenol with dichloroacetyl chloride in carbon disulphide, and of *p*-chlorophenol with benzoyl and *p*-toluoyl chloride, when the solvent is *s*-tetrachloroethane.[16]

Preferential formation of the ester—the easier reaction when possible, because the free hydroxyl group will be much more readily acylated than a ring position—is likely to be the more pronounced the lower the activity of the catalyst. For instance, in the same solvent, stannic chloride seems likely to impede esterification less than aluminium chloride.

The present work involved the use of stannic chloride in carbon tetrachloride and ethylene dichloride in the acylation of β-naphthol, *p*-methoxyphenol, and *m*-nitrophenol by both aliphatic and aromatic acid chlorides. From the considerations noted above we expected that the primary products would in all cases be largely the result of attack on oxygen, and that by proper choice of conditions it would be possible to eliminate, or render negligible, any subsequent nuclear acylation. Independent preparative-scale reactions were conducted for most of the phenol–acyl halide combinations studied kinetically, conditions similar to those found useful for the rate measurements being used. With carbon tetrachloride as solvent these preparations provided products in >87% yield in all cases. The m. p.s and infrared spectra of the products showed them to be essentially uncontaminated samples of the expected esters. These results show that at most only very small amounts of nuclear acylation could have taken place under the kinetic conditions in carbon tetrachloride, and that the reaction is probably essentially quantitative. Similar conclusions are drawn from the light-absorption measurements, for the absorption always eventually fell to that characteristic of the *O*-acylated product. For carbon tetrachloride, therefore, our expectations were realised.

In ethylene dichloride, which has a dielectric constant of 10·36 compared with 2·3 for

[14] Satchell, *J.*, 1960, 1752.
[15] Thomas, "Anhydrous Aluminium Chloride," Reinhold Publ. Corp., New York, 1941.
[16] Hayashi, *J. prakt. Chem.*, 1929, **123**, 289; Kunckell and Johannssen, *Ber.*, 1898, **31**, 169.

carbon tetrachloride, some complications were found. With β-naphthol, which was the phenol most extensively studied in carbon tetrachloride, solutions in ethylene dichloride containing also stannic chloride and acetyl chloride quickly became yellow-orange and darkened further with time. The yellow colour is discharged when a sample is run into glacial acetic acid, so that the loss of the hydroxyl band at 3300 Å may still be followed. When this is done the simple first-order behaviour found in carbon tetrachloride is not observed.

When *m*-nitrophenol—a compound likely to be less susceptible to nuclear electrophilic attack—was used rather than β-naphthol, the reaction mixtures were initially colourless, became pale yellow only after about a reaction half-life, and thereafter darkened quite slowly. Light absorption at 3300 Å again indicated slight deviation from simple first-order behaviour, and the optical densities at infinite time were somewhat greater than those expected on the assumption that *m*-nitrophenyl acetate was the only product. A preparative-scale reaction (during which any free phenols, and perhaps some of any esters present, would probably have been lost during the working-up) gave a >70% yield of *m*-nitrophenyl acetate of good m. p. (after one recrystallisation). This is clearly the main product. The deviation of the rate data from first-order behaviour begins to be significant only after 1½—2 half-lives, so a limited amount of kinetic work with this system seemed worth while. Some nuclear acylation (or other side reaction) probably occurs in this solvent, the product of which affects the light absorption. Whatever the nature of this product (unless it is a phenol, which is unlikely) it is presumably formed in rather small amounts, for otherwise an appreciable effect on the m. p. would be probable.

*Kinetics of the Reaction in Carbon Tetrachloride.*—(i). *Acylation of β-naphthol by acetyl chloride catalysed by stannic chloride.* In the main set of runs the β-naphthol concentration was *ca.* $5 \times 10^{-3}$M. The acetyl chloride concentration was varied between 0·07M and 0·56M, and the stannic chloride concentration between $0{\cdot}35 \times 10^{-3}$ and $10{\cdot}5 \times 10^{-3}$M. In the absence of stannic chloride the reaction rate was negligibly slow. For any run in the presence of the catalyst the observed loss of β-naphthol was an accurately first-order process for several half-lives. The first-order constants are collected in Table 1.

TABLE 1.

Acylation of β-naphthol by acetyl chloride in carbon tetrachloride solution at 25°.

*With an excess of acetyl chloride.* Initial [β-naphthol] ≈ $5 \times 10^{-3}$M.

(*a*) Order in stannic chloride.

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| [AcCl] | 0·14 | 0·14 | 0·14 | 0·14 | 0·14 | 0·14 | 0·14 |
| $10^3$[$SnCl_4$] | 0·35 | 0·70 | 1·05 | 1·75 | 2·10· | 4·20 | 10·5 |
| $10^3k$ (min.$^{-1}$) | 1·77 | 3·29 | 4·76 | 7·69 | 9·20 | 17·3 | 38·4 |

(*b*) Order in acetyl chloride.

| | | | | | |
|---|---|---|---|---|---|
| [AcCl] | 0·07 | 0·14 | 0·28 | 0·42 | 0·56 |
| $10^3$[$SnCl_4$] | 0·70 | 0·70 | 0·70 | 0·70 | 0·70 |
| $10^3k$ (min.$^{-1}$) | 1·19 | 3·29 | 8·65 | 16·90 | 27·6 |

*With an excess of stannic chloride.* Initial [β-naphthol] ≈ $2{\cdot}5 \times 10^{-3}$M.

| | | | |
|---|---|---|---|
| [AcCl] | 0·028 | 0·028 | 0·056 |
| $10^3$[$SnCl_4$] | 8·6 | 17·2 | 17·2 |
| $10^3k$ (min.$^{-1}$) | 5·31 | 9·33 | 19·7 |

$k$ = First-order constant. In all Tables square brackets represent molarity.

It will be seen that in the concentration ranges involved (*i.e.*, with acetyl chloride in excess of stannic chloride) the rate is of rather more than first-order in acetyl chloride and appears to increase with increasing acetyl chloride concentration (though without reaching second-order). On the other hand, the order in stannic chloride is slightly less than first (*ca.* 0·9). To test if these orders were maintained when the stannic chloride was in excess of the acetyl chloride (rather than the reverse) some experiments were carried out with *ca.* $2 \times 10^{-3}$M-naphthol (to achieve the necessary deficit compared with acetyl chloride).

The results are also in Table 1. Under such conditions the order in acetyl chloride falls too close to unity, while that in stannic chloride remains at about 0·9, perhaps falling slightly.

A number of conclusions may be drawn from these results.

(*a*) The good first-order loss of naphthol indicates that the products (hydrogen chloride and ester) do not significantly disturb the reaction. At the naphthol concentrations used this compound will be essentially unassociated, and the good first-order behaviour also indicates that reaction is with the monomers rather than with any small concentration of associated forms.[17]

(*b*) The varying order for acetyl chloride, from close to unity when in low concentration to approaching 1·7 in the most concentrated solutions studied, could imply the existence of both unimolecular and bimolecular contributions to the reaction.

(*c*) The order of slightly less than unity for stannic chloride presumably implies an essentially unimolecular engagement in the reaction, together with some other small, and at present, inexplicable effect. [In ethylene dichloride (see below) the order is effectively unity.]

Additional information was provided by a spectral study of the addition of increasing amounts of stannic chloride to a solution of β-naphthol in carbon tetrachloride. In the concentration conditions obtaining in the kinetic experiments the Lewis acid had no detectable effect on the naphthol spectrum. Therefore there is presumably little complex formation between these components in the reaction mixtures.

A mechanism compatible with the above conclusions, and also with current views concerning the Friedel–Crafts acylation and the co-ordinating ability of tin, is as shown (1—6).

(1) $AcCl + SnCl_4 \underset{}{\overset{K_1}{\rightleftharpoons}} CH_3{\cdot}\overset{\delta+}{C}O{:}\overset{\delta-}{}SnCl_4 \overset{K_2}{\rightleftharpoons} Ac^+SnCl_5^-$ (Cl on C) Fast

(2) $AcCl + CH_3{\cdot}\overset{\delta+}{C}O{:}\overset{\delta-}{}SnCl_4 \overset{K_3}{\rightleftharpoons} (CH_3{\cdot}\overset{\delta+}{C}O{:})_2\overset{\delta-}{}SnCl_4 \overset{K_4}{\rightleftharpoons} Ac^+CH_3{\cdot}\overset{\delta+}{C}O{:}\overset{\delta-}{}SnCl_5^-$ Fast (A)

(3) $Ac^+SnCl_5^- + ArOH \xrightarrow{k_1} ArO{\cdot}CO{\cdot}CH_3\ SnCl_5^-$ (H$^+$) Slow

(4) $Ac^+CH_3{\cdot}\overset{\delta+}{C}O{:}\overset{\delta-}{}SnCl_5^- + ArOH \xrightarrow{k_2} ArO{\cdot}CO{\cdot}CH_3\ CH_3{\cdot}\overset{\delta+}{C}O{:}\overset{\delta-}{}SnCl_5^-$ Slow

(5) $ArO{\cdot}CO{\cdot}CH_3\ SnCl_5^- \longrightarrow ArO{\cdot}CO{\cdot}CH_3 + HCl + SnCl_4$ (H$^+$) Fast

(6) $ArO{\cdot}CO{\cdot}CH_3\ CH_3{\cdot}\overset{\delta+}{C}O{:}\overset{\delta-}{}SnCl_5^- \longrightarrow ArO{\cdot}CO{\cdot}CH_3 + HCl + CH_3{\cdot}\overset{\delta+}{C}O{:}\overset{\delta-}{}SnCl_4$ Fast (H$^+$)

The highly charged species $(Ac^+)_2SnCl_6^-$ has been omitted from the scheme but its inclusion makes no essential difference to the subsequent argument. Dissociation of the ion pairs is unlikely to be appreciable in carbon tetrachloride and in any case the observed kinetic orders, to be compatible with the predominant participation of free ions, would require processes (5) and/or (6) (hydrogen detachment) to be rate-determining.[3] This seems unlikely. Dissociation equilibria have therefore not been included in the reaction scheme.

Oxonium and acetylium complexes have been included,[3] for both will presumably always

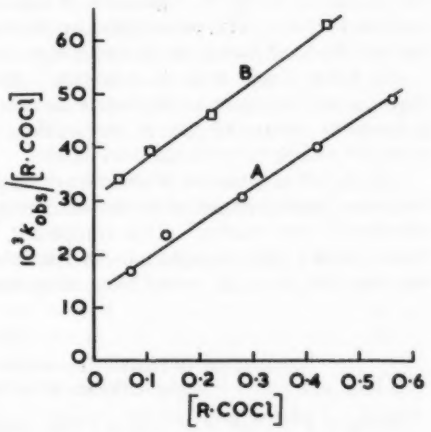
[17] Hudson and Stelzer, *Trans. Faraday Soc.*, 1958, **54**, 213.

be formed to *some* extent, even though one may largely predominate.[6b] They are both postulated as intermediates of low concentration in the present system. In the mechanism written above, only the acetylium ions are responsible for acylation. However, the concentrations of these species are simply related to those of the corresponding oxonium version by an equilibrium constant, so that the circumstance whether or not both types acts as the acetylating agent,[3,6,18] while it will affect the value of the rate constant, does not affect the essential kinetic form predicted by the proposed mechanism. This is:

$$-\mathrm{d[ArOH]}/\mathrm{d}t = (k_1[\mathrm{Ac^+SnCl_5^-}] + k_2[\mathrm{A}])[\mathrm{ArOH}]\ *$$
$$= (k_1K_1K_2[\mathrm{AcCl}][\mathrm{SnCl_4}] + k_2K_1K_3K_4[\mathrm{AcCl}]^2[\mathrm{SnCl_4}])[\mathrm{ArOH}]$$
$$= K_1[\mathrm{AcCl}][\mathrm{SnCl_4}][\mathrm{ArOH}](k_1K_2 + k_2K_3K_4[\mathrm{AcCl}])$$

or
$$k_{obs} = K_1[\mathrm{AcCl}][\mathrm{SnCl_4}](a + b[\mathrm{AcCl}])$$

In these equations square brackets represent concentration, $a$ and $b$ are constants, and $k_{obs}$ is the observed first-order rate constant. The mechanism predicts an increasing contribution to the rate from acetyl chloride as its concentration increases. At low concentrations, when $b$[AcCl] is small compared with $a$, the rate will be of the first-order in acetyl chloride; at higher concentrations the order will appear to increase, as found. The scheme may be tested by plotting $k_{obs}$/[AcCl] against [AcCl] at constant stannic chloride concentration: the Figure shows that a good straight line is obtained, as required. The data are perhaps somewhat limited, but the mechanism appears reasonable. The intermediate complexes are discussed more fully below.




Plot of $k_{obs}$/[R·COCl] against [R·COCl] for (A) acetyl and (B) propionyl chloride, with 0·70M-stannic chloride.

Kinetic results essentially similar to those found with acetyl chloride were obtained with propionyl chloride. They are given in Table 2. A graph of $k_{obs}$/[Et·COCl] against [Et·COCl] is also given in the Figure. A rectilinear plot is again obtained.

The explanation of the rising order in acetyl chloride in terms of a specific co-ordination effect, as given above, is more satisfactory than an explanation along the lines of a general solvation effect, which increases the amount of complex formation by stabilisation, though such a view is also tenable. Our preference is partly because of some results of Brown's and the effects of co-ordinating additives (both discussed below), and partly because the free stannic chloride would also be expected to participate in general solvation [12] and there is no evidence for this in the present systems.

* For A see reaction (2).

[18] Baddeley, *Quart. Rev.*, 1954, **8**, 355.

There are opportunities for various solvent effects in the above scheme. There will be the dielectric-constant effect on the equilibrium positions. The right-hand side will be favoured by increased polarity in the system. The rate-determining step, (3) and/or (4), which perhaps involves a slight dispersal of charge in the transition state (though this is not certain), will probably be rather less sensitive to increases in polarity. In practice

TABLE 2.

Acylation of β-naphthol by propionyl chloride in carbon tetrachloride solution at 25°.

| *With an excess of propionyl chloride.* Initial [β-naphthol] ≈ $5 \times 10^{-3}$M. | | | | | |
|---|---|---|---|---|---|
| [Et·COCl] | 0·05 | 0·11 | 0·22 | 0·44 | 0·11 |
| $10^3$[$SnCl_4$] | 0·70 | 0·70 | 0·70 | 0·70 | 1·75 |
| $10^3k$ (min.$^{-1}$) | 1·70 | 4·31 | 10·2 | 27·6 | 9·34 |

| *With an excess of stannic chloride.* Initial [β-naphthol] ≈ $2{\cdot}5 \times 10^{-3}$M. | | | |
|---|---|---|---|
| [Et·COCl] | 0·022 | 0·022 | 0·044 |
| $10^3$[$SnCl_4$] | 86·0 | 172 | 172 |
| $10^3k$ (min.$^{-1}$) | 9·22 | 16·0 | 36·3 |

(see below) a change to a medium of higher dielectric constant results in an appreciable increase in rate. The main influence seems likely to be on the equilibrium step. Some further effects of change in solvent composition are discussed below.

(ii) *Other Lewis acids as catalysts.* Attempts were made to use germanium tetrachloride and titanium tetrachloride as catalysts for the reaction, without success. The germanium compound proved too feeble a catalyst, and the titanium compound formed insoluble complexes with the acid halide.

(iii) *Effect of variation in structure of the phenol.* In an effort to obtain a more reactive compound than β-naphthol for use with germanium tetrachloride the behaviour of *p*-methoxyphenol was studied. This compound did prove somewhat, though not markedly, more reactive than β-naphthol. *m*-Nitrophenol was also studied, and proved *ca.* 20-fold less reactive than the *p*-methoxy-compound under the same conditions (see Table 3).

TABLE 3.

Comparison of reactivities of different phenols towards acylation by acetyl chloride in carbon tetrachloride, at 25°.

[$SnCl_4$] = $1{\cdot}75 \times 10^{-2}$M; [AcCl] = 0·14M; initial [phenol] ≈ $5 \times 10^{-3}$M.

| Phenol | β-$C_{10}H_7$·OH | *p*-MeO·$C_6H_4$·OH | *m*-$NO_2$·$C_6H_4$·OH |
|---|---|---|---|
| $10^3k$ (min.$^{-1}$) | 7·69 | 20·3 | 0·96 |

Since the slow step involves nucleophilic attack by the phenolic oxygen atom, a process which will be facilitated by electron accumulation on this atom, the rate factor is in the appropriate direction. Its comparatively small size perhaps confounds *a priori* expectations.

(iv) *Effect of variation in the structure of the acid chloride.* (1) Mechanism and a change from aliphatic to aromatic acid chloride. The results in Table 4 show that the kinetic

TABLE 4.

Acylation of β-naphthol by benzoyl chloride in carbon tetrachloride solution at 25°.

Initial [β-naphthol] ≈ $\bar{5} \times 10^{-3}$M.

| [BzCl] | 0·43 | 0·43 | 0·43 | 0·22 | 0·086 | 0·086 | 0·043 |
|---|---|---|---|---|---|---|---|
| $10^3$[$SnCl_4$] | 0·86 | 2·58 | 8·60 | 2·58 | 17·2 | 8·60 | 17·2 |
| $10^3k$ (min.$^{-1}$) | 3·97 | 10·6 | 30·0 | 3·90 | 4·90 | 2·65 | 2·46 |

pattern for acylation with benzoyl chloride has all the features found for acetyl chloride. We conclude that the mechanisms of acylation for these two compounds are basically the

same, and that minor structural modifications in either will not alter the general mechanistic outline.

(2) Effect of substituents. The following two series of acylating agents were studied. (*a*) Benzoyl and *p*-toluoyl chloride, and (*b*) chloroacetyl, acetyl, propionyl, and butyryl chloride. Comparative results are given in Table 5. For similar catalyst concentrations

TABLE 5.

Comparison of reactivities of acid chlorides as acylating agents for β-naphthol in carbon tetrachloride solution.*

| (*a*) [R·COCl] = 0·28M; [$SnCl_4$] = 0·70 × $10^{-2}$M. | | (*b*) [R·COCl] = 0·086M; [$SnCl_4$] = 8·60 × $10^{-2}$M. | |
|---|---|---|---|
| Acid chloride | $10^3k$ (min.$^{-1}$) | Acid chloride | $10^3k$ (min.$^{-1}$) |
| Acetyl | 8·65 | Acetyl | 138 |
| Propionyl | 13·8 | *p*-Toluoyl | 21·6 |
| Butyryl | 34·5 | Benzoyl | 2·65 |
| Chloroacetyl | V. slow | | |

* Small interpolations between data have been made to obtain the comparisons in this Table, which are for equivalent molarities of acylating agent.

the order of reactivity is chloroacetyl < benzoyl < *p*-toluoyl < acetyl < propionyl < butyryl. Chloroacetyl chloride was, in fact, too unreactive to give measurable rates in the present work. The obvious conclusion from the above sequence is that, within the aliphatic and probably within the aromatic series, electron-repelling substituents enhance reactivity and electron-withdrawing substituents reduce it. There is the additional fact that benzoyl chloride is less reactive than acetyl chloride. Here the structural change involved is significantly different.

There are two main ways in which substituents may affect the reaction rate, namely, by altering the position of the equilibria producing the complex intermediates, and by affecting the rate of steps (3) and/or (4).

The effect that substituents within each structurally related series are likely to have on steps (3) and (4) seems clear. Increased electron repulsion will lower the charge density on the carbonyl-carbon atom of the acyl cation, and so will hinder nucleophilic attack by the phenol and reduce the rate. Electron withdrawal will have the opposite effect. (The argument holds whichever complex is the main acylating agent.)

As regards the equilibria, electron repulsion will facilitate complex formation, and the concomitant stabilisation of the positive pole produced will retard decomposition. Hence the equilibria will shift to the right for electron-repelling substituents, and the reaction rate will be increased.

In view of the observed reactivity sequences, it is plain that in the present systems the dominant effects of substitution in benzoyl or acetyl chloride must be on the position of the equilibria (1), rather than on the slow steps.

In comparing benzoyl chloride with acetyl chloride it is difficult to predict *a priori* whether benzoyl or acetyl chloride will have the greater tendency to form complexes with a catalyst. Recent work [19] on the infrared specta for their complexes with aluminium chloride indicates that in solvents of low polarity both halides give predominantly the oxonium complex. However, acetyl chloride shows the greater tendency to give some of the acylium complex that will doubtless be the more powerful acylating agent.

If similar trends in behaviour obtain with the weaker stannic chloride, then the circumstance that benzoyl is 50 times less reactive than acetyl chloride (Table 5) can arise from a variety of factors. (*A*) Even if the acylating complex is of the same type, and formed to the same ex*tent, for both benzoyl and acetyl chloride the substitution of phenyl for methyl will reduce the charge on the carbonyl-carbon atom, by introducing conjugative relay. This will reduce the rate of step (3) or (4) for benzoylation. (*B*) The (small)

[19] Cook, *Canad. J. Chem.*, 1959, **37**, 48; Cooke, Susz, and Herschmann, *Helv. Chim. Acta*, 1954, **37**, 1280; Susz and Wuhrmann, *ibid.*, 1957, **40**, 971.

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amount of complex formation with stannic chloride may be greater for acetyl than for benzoyl chloride. (*C*) Acylation for the benzoyl compound might proceed largely *via* the oxonium complex, while an appreciable contribution from the acylium version might exist with acetyl chloride. As for the comparisons within the aromatic and the aliphatic series (see above), the resulting changes in the positions of the equilibria [effects (*B*) and (*C*)] are probably the dominant influence of the structural change. There exists a previous comparison of the reactivities of benzoyl and acetyl chlorides in a rather similar reaction:[6b] in ethylene dichloride as solvent, with aluminium chloride as catalyst, acetyl chloride is *ca.* 500 times more reactive in the acylation of toluene. However, detailed discussion of this comparison is deferred.

(v) *Kinetic consequences of changes in solvent composition.* (1) The addition of co-ordinating agents. At constant concentrations of acetyl chloride and stannic chloride,

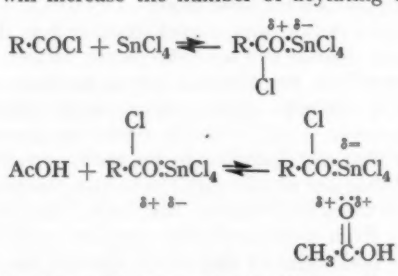
TABLE 6.

Effect of added co-ordinating agents on the stannic chloride-catalysed rate of acylation of β-naphthol by acetyl chloride in carbon tetrachloride.

| (*a*) Ethyl ether. | | | | (*b*) Acetic acid. | | | |
|---|---|---|---|---|---|---|---|
| [AcCl] | $10^3$[$SnCl_4$] | [$Et_2O$] | $10^3k$ (min.$^{-1}$) | [AcCl] | $10^3$[$SnCl_4$] | [AcOH] | $10^3k$ (min.$^{-1}$) |
| 0·14 | 1·75 | 0·00 | 7·69 | 0·14 | 0·35 | 0·00 | 1·77 |
| 0·14 | 1·75 | 0·048 | 11·1 | 0·14 | 0·35 | 0·55 | 19·2 |
| 0·14 | 1·75 | 0·19 | 17·3 | 0·14 | 0·35 | 0·88 | 19·2 |
| 0·14 | 1·75 | 0·48 | 15·0 | 0·14 | 0·35 | 1·75 | 16·4 |
| 0·14 | 1·75 | 0·96 | 10·5 | 0·14 | 0·00 | 1·75 | V. slow |

the addition of increasing quantities of ethyl ether or of anhydrous acetic acid at first increases the reaction rate, but eventually reduces it. The concentration at which the rate is a maximum is approximately the same for ether and acetic acid, though the enhancement is more marked for the latter. Some experimental results are given in Table 6.

Since, even in the presence of additives, the rate without catalyst remains negligibly small, the rate enhancements are not to be explained as uncatalysed contributions. However, by bearing in mind the essentials of the proposed mechanism (p. 5408) and the well-established ability of stannic chloride to form complexes with oxygen-containing compounds, it seems possible to rationalise the observations. Stannic chloride forms particularly stable compounds with both ether[20] and acetic acid,[21] and their addition to the solvent therefore provides species which compete with the acetyl chloride for the catalyst. Eventually the additives will tend to monopolise the catalyst, and the rate will fall. Initially, however, they may increase the formation of an active complex by taking the part played by the second molecule of acid chloride in the doubly co-ordinated complexes. This process will increase the number of acylating complexes until such a



time as the strongly co-ordinating additives seriously displace the acid chloride molecules from contact with the catalyst. The details of the effect will vary with the additive, the

[20] See, *e.g.*, Bell and Skinner, *J.*, 1952, 2955.
[21] Satchell, *J.*, 1958, 3910, and references therein.

solvent, and other conditions. (This interpretation of the effect of co-ordinating agents is superficially at variance with Baddeley's.[18] This author sees additives as reducing the electrophilic character of any cations involved, by partial satisfaction of their electron demand, thus causing a fall in reaction rate. While a loss of electrophilicity is no doubt incurred, nevertheless it seems that in the present system the beneficial effect on the displacement of the complex-forming equilibria outweighs this loss. For systems where complex formation is quantitative the loss of electrophilicity must be a factor in the inhibition produced by additives, but we agree with Jensen and Brown [3] in thinking the most important effect, even then, to be competition for the catalyst.)

If a prominent effect of the additives is the extra co-ordination provided for the acetyl chloride complexes, as suggested above, and if the interpretation of the high and fractional orders in acetyl chloride is correct, then, with sufficient ether or acetic acid present, the order in acetyl chloride should be noticeably reduced, eventually falling to unity. This is the case. Results in Tables 7 and 8 indicate a less pronounced dependence on acetyl

TABLE 7.

Order in acetyl chloride in presence of added ethyl ether.

| [AcCl] | $10^3$[$SnCl_4$] | [$Et_2O$] | $10^3k$ (min.$^{-1}$) | [AcCl] | $10^3$[$SnCl_4$] | [$Et_2O$] | $10^3k$ (min.$^{-1}$) |
|---|---|---|---|---|---|---|---|
| 0·035 | 1·75 | 0·48 | 2·88 | 0·14 | 1·75 | 0·48 | 15·0 |
| 0·07 | 1·75 | 0·48 | 6·17 | 0·28 | 1·75 | 0·48 | 36·1 |

TABLE 8.

Order in acetyl chloride in presence of added acetic acid.

| [AcCl] | $10^3$[$SnCl_4$] | [AcOH] | $10^3k$ (min.$^{-1}$) | [AcCl] | $10^3$[$SnCl_4$] | [AcOH] | $10^3k$ (min.$^{-1}$) |
|---|---|---|---|---|---|---|---|
| 0·07 | 0·35 | 1·75 | 8·13 | 0·28 | 0·35 | 1·75 | 34·4 |
| 0·14 | 0·35 | 1·75 | 16·4 | 0·56 | 0·35 | 1·75 | 76·7 |

chloride concentration in the presence of 0·48M-ether, and an essentially first-order dependence in the presence of 1·75M-acetic acid. The latter compound has already been noted as producing the more marked effects. These results help to produce confidence in the overall mechanistic picture.

(2) Change in dielectric constant. As previously argued, a general increase in polarity of the solvent, without necessarily an increase in specific co-ordinating ability, could affect the reaction rate in two ways. The equilibria forming the ionic complexes will be favoured, and this will tend to increase the rate. On the other hand, the effect on the rate-determining step is somewhat ambiguous, but, in any case, likely to be less important. In practice a change from carbon tetrachloride (dielectric constant $\approx$ 2·3) to ethylene dichloride (dielectric constant $\approx$ 10·4) increases the rate of reaction between *m*-nitrophenol and acetyl chloride *ca.* 20-fold.

TABLE 9.

Acylation of *m*-nitrophenol in ethylene dichloride solution catalysed by stannic chloride at 25°.

Initial [*m*-nitrophenol] $\approx 5 \times 10^{-3}$M.

(a) *Acylation by acetyl chloride.*

| [AcCl] | $10^3$[$SnCl_4$] | $10^3k$ (min.$^{-1}$) |
|---|---|---|
| 0·07 | 0·88 | 3·56 |
| 0·14 | 0·88 | 9·86 |
| 0·28 | 0·88 | 25·6 |
| 0·14 | 1·76 | 20·3 |
| 0·14 | 2·64 | 28·8 |

(b) *Acylation by benzoyl chloride.*

| [BzCl] | $10^3$[$SnCl_4$] | $10^3k$ (min.$^{-1}$) |
|---|---|---|
| 0·086 | 8·6 | 19·1 |

Because of the somewhat unsatisfactory nature of the reaction in ethylene dichloride (see above) rather little work was performed with this solvent. The results in Table 9 reveal, however, that the kinetic pattern must be very similar to that obtaining in carbon

tetrachloride. It is interesting that the order in stannic chloride seems essentially unity in this medium. The order in acyl halide is still greater than unity in spite of the increase in polarity. This is presumably because the medium has not the *specific* solvating power of the acyl halide—indeed specific co-ordination effects could well be enhanced by the raised dielectric constant. In the concentration ranges studied, stannic chloride and *m*-nitrophenol did not appear to interact (as judged by measurements of ultraviolet absorption), so this possible complication was still absent.

In a single experiment, acetyl chloride proved *ca.* 25-fold more reactive than benzoyl chloride in this system. This value compares with a factor of about 50 obtained in carbon tetrachloride (though with a different phenol—β-naphthol).

*Previous Mechanistic Conclusions and the Present Work.*—Previous kinetic work on the acylation of aromatic compounds in solvents of low polarity has largely concerned aluminium chloride. This catalyst forms, even in ethylene dichloride, stable 1 : 1 complexes with, for example, benzoyl chloride and acetyl chloride,[6] in which the equilibrium position lies towards the complex side. Indeed it is common to pre-form the complex and add it as such. The ketone product also engages the catalyst, and so largely removes it from its useful sphere of influence. Thus reactions under such conditions [6] are usually of the first order in catalyst–acyl halide complex and of the first order in aromatic substrate. Reasonable excesses of acyl halide over catalyst have generally little effect on the reaction rate, the catalyst being already fully co-ordinated (the usual co-ordination number for aluminium is four). An excess of catalyst over acyl halide enhances the rate because it enables 1 : 2 complexes (*i.e.*, those containing the very active $Al_2Cl_6$ combination) to increase in number. The effect of changes in dielectric constant are not clear cut.[6a]

These results are in harmony with the traditional conception of the reaction; those now obtained with stannic chloride as catalyst do not fit it so well. This Lewis acid does not give quantitative formation of complexes with common acyl halides [3] nor, in the present case, does it form complexes appreciably with the products. The kinetics are therefore different from those with aluminium chloride. There will be free stannic chloride and free acyl halide at all relative concentrations of these substances, and the small extent of interaction between them involves complexes containing both one and two molecules of acyl halide. The reaction does not suffer the usual eventual marked reduction in rate owing to engagement of catalyst by products, though it might do so if the products were in great excess over the catalyst.

The effect of an increase in dielectric constant is to facilitate the reaction considerably.

The essentials of the mechanism for aluminium chloride catalysis can be written as:

$$R{\cdot}COCl + AlCl_3 \longrightarrow R{\cdot}C(Cl)=O^{\delta+}{:}AlCl_3^{\delta-} \rightleftharpoons [R{\cdot}CO]^+[AlCl_4]^- \quad \text{Fast}$$

$$[R{\cdot}CO]^+[AlCl_4]^- + ArH \longrightarrow \text{Products} \quad \text{Slow}$$

where $R{\cdot}CO^+AlCl_4^-$ is probably present in greater amounts for acetyl than for benzoyl chloride [19] but where oxonium complex formation is probably essentially quantitative for both.[6] Quite how much acylium complex is likely to be present is not clear. If the oxonium complex is chiefly responsible for acylation in either the aliphatic or the aromatic series, then electron-repelling substituents should reduce the reaction rate owing to their reduction of the positive charge carried by the carbonyl carbon atom of the stoicheiometrically formed acylating agent. However, if the rate were increased, this would imply that the acylium complexes are playing a significant rôle, for their concentrations will be increased by such substituents. Brown's promised data on substituted benzoyl chlorides are therefore awaited with interest.[6a]

Finally, the above considerations of the differences of mechanistic detail make it clear that the relative reactivities of any two acyl halides may well be different when used with

stannic chloride and when used with aluminium chloride. The only comparison available is that concerning benzoyl and acetyl chloride, which is particularly complicated from the interpretative viewpoint (see above). For stannic chloride we find a reactivity ratio of *ca.* 25; Brown and his collaborators [65] found one of *ca.* 500 for aluminium chloride. Thus a notable difference in reactivity is indeed found for this case.

On the whole, available studies indicate that further progress in the understanding of the complexities of Friedel–Crafts acylation are now most likely to come from detailed work with individual catalysts, and that generalities embracing several catalysts are likely to prove invalid. From this viewpoint reviews dealing with the properties of particular Lewis acids are especially welcome.[22]

KING'S COLLEGE, STRAND, LONDON, W.C.2. [*Received, June 5th,* 1961.]

[22] Shiihara, Swartz, and Post, *Chem. Rev.*, 1961, **61**, 1; Topchiev, Zavgorodnii, and Paushkin, "Boron Trifluoride and its Compounds as Catalysts in Organic Chemistry," Pergamon Press, London, 1959.

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## 1066. *Optical Rotatory Dispersion. Part II.*[1] *3-Monohydroxy-steroids, 3,17-Dihydroxy-steroids, and their Derivatives.*

By W. KLYNE and P. MARSHALL-JONES.

Rotatory-dispersion curves of complete series of isomeric androstan-3-ols and of androstane-3,17-diols and their derivatives have been determined.

The results for the 3,17-diols and their derivatives are compared with those calculated from the data for the corresponding 3- and 17-mono-substituted compounds; interaction of groups at positions 3 and 17 is assessed.

THE first paper of this series [1] described the determination of the rotatory-dispersion curves of complete series of 17- and 20-monosubstituted steroids. It was shown that non-ketonic substituents in a steroid molecule make a marked contribution to the rotatory-dispersion curve of the compound. These contributions vary, not only with the nature of the substituent, but also with the position and configuration of substitution in the nucleus.

This paper describes, first, the results obtained with two complete series of 5α- and 5β-androstan-3-ols, their acetates, and their benzoates. All the curves considered are plain (for nomenclature, see ref. 2) since the spectral range studied (600—300 mμ) does not include an absorption band.

We then describe the results obtained from rotatory-dispersion studies of all the isomeric 3,17-diols of both the 5α- and 5β-androstane series, together with their diacetates and dibenzoates. For a di- or poly-substituted steroid the total rotation at any given wavelength may be considered as the arithmetical sum of the rotation contributions of the steroid nucleus and of each substituent. For some compounds the "calculated" results obtained by simple addition of these contributions do not agree with the experimental results. These discrepancies must be due to long-range interaction of the substitutents.

Such interaction of substituents has been studied extensively for "monochromatic" molecular-rotation differences ($[M]_D$ values; for reviews see refs. 3 and 4). One of the objects of this work was to test how far the complete rotatory-dispersion curves for

[1] Part I, Jones (now Marshall-Jones) and Klyne, *J.*, 1960, 871.
[2] Djerassi and Klyne, *Proc. Chem. Soc.*, 1957, 55.
[3] Barton and Klyne, *Chem. and Ind.*, 1948, 755.
[4] Klyne, in "Determination of Organic Structures by Physical Methods," ed. Braude and Nachod, Academic Press, New York, 1955.

substituents are additive. In the case of 3,17-disubstituted steroids it was thought that, as the two substituents were at opposite ends of the molecule there would be little chance of reaction between them, and the dispersion curves should be simply additive.

" Calculated " dispersion curves were obtained for each compound in the series by adding together the curves of the corresponding monosubstituted compounds, and subtracting the " background " curve for the corresponding hydrocarbon. The subtraction was necessary, since otherwise the " background " would be included twice. Each " calculated " curve was then compared with the experimental curve for the same compound.

In Part I [1] we discussed the graphical analysis of the results for 17- and 20-monosubstituted steroids to obtain equations of the Drude type. A similar analysis of the results in the present paper was carried out, but since the general conclusion (as in Part I) was that for many structural studies the calculation of Drude equation constants is not worth the labour involved, we omit the details here (see ref. 5).

*Units and Symbols.*—Wavelength ($\lambda$) is in m$\mu$. For molecular rotation we have

$$[\phi] = [\alpha] \times \text{mol. wt.}/100.$$

## Results

All compounds were studied in methanol solution from 600 to 300 m$\mu$; all the curves were plain curves, and with one exception did not change sign within the range measured.

3- *and* 17-*Monosubstituted Compounds.*—Table 1 gives the molecular rotations at 600, 500, and 300 m$\mu$ for the isomeric androstan-3-ols and their acetates and benzoates. It is apparent that most of the differences between the curves for corresponding alcohols, acetates, and

Table 1.

Rotatory dispersion data for 3- and 17-monosubstituted androstane derivatives.

Curves were measured for methanol solutions from 600 to 300 m$\mu$. All are plain curves and do not change sign, except those marked *.
Values given are molecular rotations [$\phi$] at 600, 500, and 300 m$\mu$ (in that order).

| Androstane deriv. | 5$\alpha$-Series | 5$\beta$-Series | Androstane deriv. | 5$\alpha$-Series † | 5$\beta$-Series |
|---|---|---|---|---|---|
| 3$\alpha$-OH | +50°, 60°, 190° | +50°, 90°, 310° | 17$\alpha$-OH | −25°, 45°, 150° | −80°, 90°, 270° |
| 3$\beta$-OH | +25, 30, 70 | +35, 40, 150 | 17$\beta$-OH | +30, 50, 140 | +70, 70, 200 |
| 3$\alpha$-OAc | +80, 95, 160 | +140, 180, 150 | 17$\alpha$-OAc | +10, 10, 80 | Not available |
| 3$\beta$-OAc | −35, 40, 220 | −5, 5, 70 | 17$\beta$-OAc | +150, 60, −380 | ,, ,, |
| 3$\alpha$-OBz | −40, 40, 310 | +60, 100, 350 | 17$\alpha$-OBz | −240, 310, 1270 | −190, 220, 1130 |
| 3$\beta$-OBz | −25, 5, +220 * | +110, 150, 420 | 17$\beta$-OBz | +210, 310, 1710 | +180, 320, 1800 |

* [$\phi$] is at 0° at 460 m$\mu$. † Repeated from ref. 1 for comparison.

benzoates of the 3-mono-substituted series are relatively small, even at low wavelengths. This is in marked contrast to the curves for the 17- and 20-monosubstituted compounds,[1] for which the benzoate curves, in particular, diverge widely from those of the corresponding alcohols. The molecular rotations at 300 m$\mu$ for 17- and 20-monobenzoates are of the order of $\pm$1000°; this difference is probably a reflection of the fact that in the 3-substituted compounds the CH·OBz group is separated from asymmetric centres on either side by methylene groups, whereas in the 17- and 20-substituted series it is immediately adjacent to an asymmetric centre (cf. Stokes and Bergmann [6]).

Table 1 also gives some data for 17-substituted androstanes (cf. ref. 1).

3,17-*Disubstituted Compounds.*—Table 2 gives the observed molecular rotations at 600, 500, and 300 m$\mu$ for the isomeric androstane-3,17-diols, their diacetates, and dibenzoates, and the corresponding calculated rotations. The rotation contributions of substituents at $C_{(3)}$ are relatively small (see above), whereas those of substituents at $C_{(17)}$ are large.[1] The sign and shape of the dispersion curves of the 3,17-disubstituted compounds are thus dominated by the

[5] Jones, M.Sc. Thesis, London, 1959.
[6] Stokes and Bergmann, *J. Org. Chem.*, 1952, **17**, 1194.

TABLE 2.

Rotatory dispersion data for 3,17-disubstituted androstane derivatives.

For notes see Table 1.

| | Observed | | | Calculated | | |
|---|---|---|---|---|---|---|
| 5α-Androstane-3α,17α-diol | −25°, | 25°, | 210° | +20°, | 5°, | 0° |
| ,, -3α-17β- ,, | +85, | 95, | 250 | +75, | 100, | 290 |
| ,, -3β,17α- ,, | −75, | 100, | 220 | −5, | 25, | 120 |
| ,, -3β,17β- ,, | 0, | +20, | 125 | +50, | 70, | 170 |
| 5β-Androstane-3α,17α- ,, | 0, | −15, | 65 | −30, | 0, | +40 |
| ,, -3α,17β- ,, | +95, | 115, | 295 | +120, | 160, | 510 |
| ,, -3β,17α- ,, | −40, | 70, | 260 | −45, | 50, | 120 |
| ,, -3β,17β- ,, | +50, | 60, | 170 | +105, | 110, | 350 |
| 5α-Androstane-3α,17α-diol diacetate | +30, | 40, | 120 | +85, | 95, | 200 |
| ,, -3α,17β- ,, | +95, | 110, | 320 | +225, | 145, | −260 |
| ,, -3β,17α- ,, | +20, | 20, | 20 | −30, | 40, | 180 |
| ,, -3β,17β- ,, | −45, | 60, | 180 | +110, | 10, | −640 |
| 5β-Androstane-3α,17α- ,, | +120, | 190, | 680 | +150, | 190, | 230 |
| ,, -3α,17β- ,, | +160, | 260, | 680 | +290, | 240, | −230 |
| ,, -3β,17α- ,, | +80, | 110, | 220 | +5, | 5, | 10 |
| ,, -3β,17β- ,, | +100, | 120, | 260 | +145, | 55, | −450 |
| 5α-Androstane-3α,17α-diol dibenzoates | +110, | 150, | 680 * | −285, | 360, | 1620 * |
| ,, -3α,17β- ,, | +390, | 510, | 2780 | +165, | 260, | 1360 |
| ,, -3β,17α- ,, | −120, | 170, | 720 | −270, | 325, | 1090 |
| ,, -3β,17β- ,, | +200, | 320, | 1660 | +180, | 295, | 1890 |
| 5β-Androstane-3α,17α- ,, | +90, | 170, | 1460 * | −130, | 120, | 780 * |
| ,, -3α,17β- ,, | +380, | 710, | 3980 | +240, | 420, | 2150 |
| ,, -3β,17α- ,, | −160, | 170, | 780 | −80, | 70, | 710 |
| ,, -3β,17β- ,, | +190, | 300, | 1460 | +290, | 470, | 2220 |

* See text.

effects of the 17-substituents. As might have been expected, discrepancies between observed and calculated curves are often greater for compounds containing the bulkier and more polarisable acetate and benzoate groups than for the hydroxy-compounds.

Two compounds show such large differences between observed and calculated curves as to merit special attention; these are 5α- and 5β-androstane-3α,17α-diol dibenzoates. For both the observed curves are strongly positive but the calculated curves are strongly negative. The observed results were checked twice, and the identity of the 5β-dibenzoate (a new compound) was checked by hydrolysis to the known diol and by an alternative synthesis. 17α-Hydroxy-5β-androstan-3-one was converted into its benzoate, which was then reduced with sodium borohydride to 17α-benzoyloxy-5β-androstan-3α-ol. The dispersion curve of this monobenzoate was in good agreement with the calculated curve. This confirms the fact that no alteration in configuration at $C_{(17)}$ has taken place. The monobenzoate was finally benzoylated, giving material identical with the previous sample of dibenzoate (m. p., mixed m. p., and dispersion curve). It can only be suggested that these grossly anomalous results may be due to the dibenzoates taking up an abnormal conformation, *e.g.*, a boat form of ring A or some other flexible form intermediate between chair and boat such as the " twist " conformation proposed by Johnson *et al.*[7]

## EXPERIMENTAL

Optical rotations were determined with a Rudolph photoelectric spectropolarimeter as described in Part I [1] (tube, 1 dm.; 18—22°; 1 mg./c.c.).

*Compounds.*—These were made by standard methods from materials generously supplied for the M.R.C. Steroid Reference Collection by the pharmaceutical industry. The m. p. (corrected) and molecular rotations [$\phi$] of chloroform solutions (measured with a visual polarimeter) are listed below in that order. Previous references to most compounds are given in Elsevier's " Encyclopædia " [8] and by Mathieu and Petit.[9]

3-*Monosubstituted Compounds.*—5α-Androstane derivatives: 3α-OH, 146—148°, +6°; 3β-OH, 148—150°, +3°; 3α-OAc, 130—131°, +10°; 3β-OAc, 70—72°, −40° (Butenandt *et al.*[10]

[7] Johnson, Baver, Margrave, Frisch, Dreger, and Hubbard, *J. Amer. Chem. Soc.*, 1961, **83**, 606.
[8] Elsevier's " Encyclopaedia of Organic Chemistry," Vol. XIV, 1940, and Supplement, Amsterdam, 1954.
[9] Mathieu and Petit, " Pouvoir Rotatoire Naturel," Tome I, " Steroïdes," Masson, Paris, 1956.
[10] Butenandt, Poschmann, Failer, Schiedt, and Biekert, *Annalen*, 1951, **575**, 123.

give m. p. 87—88° for the unsolvated compound); 3α-OBz, 149—150°, −14°; 3β-OBz, 146—148°, −8°; 5β-Androstane derivatives: 3α-OH, 145—146°, +29° (Prelog *et al.*[11] give +19°); 3β-OH, 143—144°, +6°; 3α-OAc, 110—111°, +91°; 3β-OAc, gum, +7°; 3α-OBz, 105—106°, +73°; 3β-OBz, 170—172°, +36°.

New compounds are: 5α-* (Found: C, 77·6; H, 10·7. $C_{21}H_{34}O_2,\frac{1}{2}CH_3{\cdot}OH$ requires C, 77·2; H, 10·8%) and 5β-*androstan*-3α-*yl acetate* * (Found: C, 77·8; H, 10·9%); 5α-*androstan*-3α- (Found: C, 82·0; H, 9·8. $C_{26}H_{36}O_2$ requires C, 82·1; H, 9·55%) and -3β-*yl benzoate* (Found: C, 81·9; H, 9·7%); 5β-*androstan*-3α- (Found: C, 82·4; H, 9·2%) and -3β-*yl benzoate* (Found: C, 81·8; H, 9·25%).

3,17-*Disubstituted Compounds.*—5α-*Androstane derivatives.* Diols: 3α,17α-, 229—230°, −40°; 3α,17β-, 224—225°, +55°; 3β,17α-, 221—222°, −21°; 3β,17β-, 167—168°, +16°. Diacetates: 3α,17α-, gum, (sample lost); 3α,17β-, 161—162°, +64°; 3β,17α-, 145—146°, −42°; 3β,17β-, 127—128°, +4°. Dibenzoates: 3α,17α-, gum, +110°; 3α,17β-, 209—210°, +346°; 3β,17α-, 185—186°, −101°; 3β,17β-, 198—200°, +188°.

5β-*Androstane derivatives.* Diols: 3α,17α-, 227—228°, −7°; 3α,17β-, 233—235°, +73°; 3β,17α-, 216—217°, −35°; 3β,17β-, 150—153° and 165—166° (these appear to be different crystalline forms; cf. ref. 12), +49°. Diacetates: 3α,17α-, 75—76°, 0°; 3α,17β-, 123—124°, +137°; 3β,17α-, 159—160°, +1°; 3β,17β-, 112—113°, +21°. Dibenzoates: 3α,17α-, 213—214°, +105°; 3α,17β-, 163—164°, +462°; 3β,17α-, 186—188°, −107°; 3β,17β-, 147—148°, +196°.

New compounds are: 5β-*androstane*-3β,17α- (Found: C, 73·5; H, 9·6. $C_{23}H_{36}O_4$ requires C, 73·4; H, 9·60%), and 3β,17β-*diol diacetate* (Found: C, 73·2; H, 9·8%); 5α-*androstane*-3α,17β- (Found: C, 79·5; H, 7·6. $C_{33}H_{40}O_4$ requires C, 79·2; H, 8·05%), 3β,17α- (Found: C, 79·3; H, 8·0%), and -3β,17β-*diol dibenzoate* (Found: C, 79·1; H, 7·9%); 5β-*androstane*-3α,17α- (Found: C, 78·9; H, 7·9%), -3α,17β- (Found: C, 79·4; H, 8·0%), -3β,17α- (Found: C, 79·6; H, 8·35%), and -3β,17β-*diol dibenzoate* (Found: C, 79·1; H, 8·1%).

This work was financed in part by a contract from the U.S. Army Research and Development Group in Frankfurt-am-Main, and by a grant from the Department of Scientific and Industrial Research. The Rudolph polarimeter and ancillary equipment were a generous loan from the Wellcome Trust. We are indebted for the loan of other apparatus to Imperial Chemical Industries Limited and for gifts of steroids to Messrs. Parke Davis and Co., Detroit, Mich., British Drug Houses Ltd., and Ciba A.-G., Basle.

Medical Research Council, Steroid Reference Collection.
Westfield College, London, N.W.3. [*Received, June 7th*, 1961.]

* These compounds have not been obtained unsolvated; see Jones [8] for full discussion.

[11] Prelog, Ruzicka, Meister, and Wieland, *Helv. Chim. Acta*, 1945, **28**, 618.
[12] Fieser and Wei-Yuan Huang, *J. Amer. Chem. Soc.*, 1953, **75**, 4837.

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## 1067. N-*Alkylated* 5-*Fluorotryptamines.*

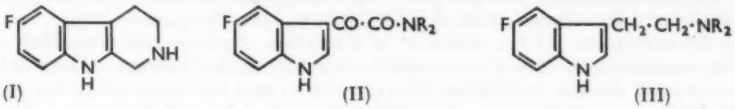
By Z. Pelchowicz, A. Kaluszyner, and M. Bentov.

A new synthesis of 5-fluoroindole from 3-fluorotoluene is described. Through condensation with oxalyl chloride, reaction with secondary amines, and reduction, *N*-alkyl-5-fluorotryptamines have been prepared.

The biological properties of *N*-alkyl-tryptamines have recently aroused interest,[1] in particular, 5-hydroxy-*NN*-dimethyltryptamine (bufotenin) which produces hallucinations and intoxication. Seeds of *Piptadenia peregrina* and *macrocarpa* which contain this base and its hydroxyl-free analogue, have been used for centuries by the natives of South America for ceremonial purposes.[2] In view of the biological properties conferred upon

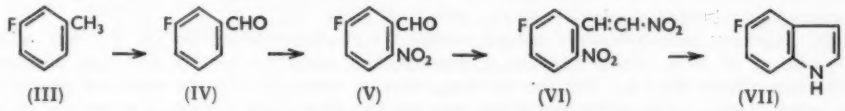
[1] See, *e.g.*, Hearst and Szara, *Amer. Psychologist*, 1960, **15**, 476; Gessner, McIsaac, and Page, *Nature*, 1961, **190**, 179.
[2] Manske, "The Alkaloids," Academic Press, New York and London, 1960, Vol. VII, p. 5.

tryptophan by $C_{(5)}$-fluorination,[3] *NN*-dialkyl derivatives (III) of 5-fluorotryptamine have been synthesised. 5-Fluorotryptamine,[4] upon treatment with formaldehyde and formic




acid, did not yield a methyl derivative but a compound believed to be 6-fluoro-1,2,3,4-tetrahydronorharmaline (I), by analogy with the reaction between 5-fluorotryptamine and acetaldehyde [5] and in view of the similarity of the infrared spectra of the two substances. Speeter and Anthony's method [6] was, therefore, used for the synthesis of the tryptamine (III).* 5-Fluoroindole reacted smoothly with oxalyl chloride; the resulting chloride was treated with dimethylamine or diethylamine, and the products (II) were reduced with lithium aluminium hydride in ether–tetrahydrofuran. The desired bases (III; R = Me or Et) were isolated as their hydrochlorides.

The known methods for the synthesis of 5-fluoroindole (VII) [7,8] did not lend themselves to large-scale preparations. The following four-step method gave an overall yield of 29%, starting from 3-fluorotoluene:




For the conversion of 3-fluorotoluene into 3-fluorobenzaldehyde (IV),[9] chlorination to 3-fluorobenzylidene chloride and subsequent hydrolysis appear to be preferable to oxidation with chromic anhydride. Nitration of the aldehyde [9] can be carried out either with nitric acid and sulphuric acid (at the stage of the diacetate) or with sulphuric acid and potassium nitrate; both of these methods are superior to the nitration with nitric acid in acetic anhydride. The reduction of 5-fluoro-2,ω-dinitrostyrene (VI), easily obtained from the nitrated aldehyde (V) and nitromethane,[10] is best carried out catalytically,[11] in ethyl acetate–acetic acid as solvent; inferior results were obtained with iron in acetic acid–ethanol.[12]

## Experimental

*6-Fluoro-1,2,3,4-tetrahydronorharmaline* (I).—A mixture of 5-fluorotryptamine hydrochloride (10 g.), 36% formaldehyde solution (7·8 g.), 88% formic acid (6·0 g.), and sodium carbonate (2·5 g.) was refluxed gently for 5 hr., cooled, diluted, and neutralized. The *product* (8·5 g.) was insoluble in ether and water, soluble in hot hydrochloric acid, and had m. p. 226—228° (from ethanol) (Found: F, 10·4; N, 14·7. $C_{11}H_{11}FN_2$ requires F, 10·0; N, 14·7%).

*3-Fluorobenzaldehyde* (IV).—(*a*) A stream of chlorine was passed through boiling and strongly illuminated 3-fluorotoluene (110 g.), until *ca.* 70 g. were absorbed and the internal temperature had reached 195°. The resulting *3-fluorobenzylidene chloride* had b. p. 202—204°, $n_D^{16}$ 1·5304, $d_{16}^{16}$ 1·360, $M_R$, 40·70 (Calc.: 40·40) (Found: C, 46·6; H, 3·1; F, 10·7. $C_7H_5Cl_2F$ requires C, 46·9; H, 2·8; F, 10·6%). The crude 3-fluorobenzylidene chloride was refluxed for

* In a recent paper [5] we overlooked the fact that 7-methyltryptamine had been prepared by the same method before (Abramovitch *et al.*, *J.*, 1951, 847).

[3] See, *e.g.*, Sharon and Lipmann, *Arch. Biochem. Biophys.*, 1957, **69**, 219.
[4] Pelchowicz and Bergmann, *J.*, 1959, 847.
[5] Pelchowicz and Bergmann, *J.*, 1960, 4699.
[6] Speeter and Anthony, *J. Amer. Chem. Soc.*, 1954, **76**, 6208.
[7] Allen, Brunton, and Suschitzky, *J.*, 1955, 1283.
[8] Bergmann and Pelchowicz, *J.*, 1959, 1913.
[9] Schwarcz, Ph.D. Thesis, University of Buenos Aires, 1955.
[10] Huebner, Troxell, and Schroeder, *J. Amer. Chem. Soc.*, 1953, **75**, 5887.
[11] Benington, Morin, and Clark, *J. Org. Chem.*, 1960, **25**, 1542.
[12] A.Ek and B. Witkop, *J. Amer. Chem. Soc.*, 1954, **76**, 5579.

5 hr. with calcium carbonate (500 g.) and water (1·2 l.), and the organic material was steam distilled and then extracted with ether. The extract was washed with dilute sodium carbonate solution, dried, and distilled. The *aldehyde* (87 g.; 70%) boiled at 80—81°/30 mm. From the alkaline washings 3-fluorobenzoic acid (8 g., 6%), m. p. 123—125°, was isolated.

(*b*) To 3-fluorotoluene (71 g.), dissolved in a mixture of acetic anhydride (500 ml.) and acetic acid, sulphuric acid (230 g.) was added while cooling and stirring. The solution was cooled to −5°, and chromic anhydride (130 g.) added so that the temperature did not exceed 10°. The stirring was continued at room temperature for 1 hr. and the product poured into ice–water and filtered off. 3-*Fluorobenzylidene diacetate* (106 g., 73%) crystallized from light petroleum (b. p. 60—90°) and melted at 40° (Found: F, 8·1. $C_{11}H_{11}FO_4$ requires F, 8·4%).

5-*Fluoro*-2-*nitrobenzaldehyde* (V).—(*a*) *Acetic anhydride–nitric acid method.* A solution of 3-fluorobenzaldehyde (77·5 g.) in acetic anhydride (190 ml.) was slowly mixed with a cold solution of concentrated sulphuric acid (8 ml.) in acetic anhydride (380 ml.), and nitric acid (155 ml., *d* 1·50) added, dropwise and with stirring, at 20—30° during 40 min. The stirring was continued for 3 hr. and the solution then poured on crushed ice (2 kg.) and partially neutralized with 30% sodium hydroxide solution. The yellowish precipitate (105 g., 62%) was washed with cold water, triturated with cold ethanol, filtered off, and dried. 5-*Fluoro*-2-*nitrobenzaldehyde diacetate* (105 g., 62%), after recrystallization from ethanol, had 90—91° (Found: C, 48·2; H, 4·1; F, 6·9; N, 5·4. $C_{11}H_{10}FNO_6$ requires C, 48·7; H, 3·8; F, 7·0; N, 5·2%). The crude diacetate was hydrolysed by refluxing it for 1 hr. with concentrated sulphuric acid (30 ml.) in 50% ethanol (550 ml.). The solution was cooled and filtered to give 5-fluoro-2-nitrobenzaldehyde (V) (60·5 g., 57%), m. p. 94—95°.

(*b*) *Sulphuric acid–potassium nitrate method.* 3-Fluorobenzaldehyde (87 g.) was added dropwise at 0° to a stirred mixture of concentrated sulphuric acid (1 kg.) and powdered potassium nitrate (74·5 g.), and the resulting solution stirred for 15—20 min. and poured on ice–water (3 kg.). The white precipitate was washed thoroughly with cold water and dried. The aldehyde so obtained (108 g., 91%) melted at 93—95° and was sufficiently pure.

(*c*) *Sulphuric acid–nitric acid method.* 3-Fluorobenzaldehyde diacetate (70 g.) was added during 5 min. and with good agitation to concentrated sulphuric acid (250 ml.), cooled to −5°. The temperature rose to 2°. The stirring was continued for 10 min. and nitric acid (100 ml., *d* 1·52) added gradually between −10 and 0°. The temperature was permitted to reach 14° and the mixture was then poured on crushed ice. The product (48·5 g., 88%) formed yellowish needles (from dilute ethanol), m. p. 94°.

5-*Fluoro*-2,ω-*dinitrostyrene* (VI).—To a stirred mixture of the fluoronitrobenzaldehyde (V) (55 g.), nitromethane (18 g.), and methanol (80 ml.), cooled to −18°, sodium hydroxide (13·6 g.) in water (20 ml.) was added slowly so that the temperature did not exceed 10°. The stirring was continued for 1 hr. at 10—15° (if the solution had become too viscous, more methanol was added) and the mixture poured into ice–water (250 ml.). The clear solution was stirred quickly into a mixture of water (80 ml.) and concentrated hydrochloric acid (80 ml.). 1-(5-*Fluoro*-2-*nitrophenyl*)-2-*nitroethanol*, was filtered off. A sample was recrystallized from chloroform–light petroleum and melted at 93—94° (Found: C, 42·1; H, 3·0; F, 8·0. $C_8H_7FN_2O_5$ requires C, 41·8; H, 3·0; F, 8·3%).

The alcohol was refluxed for 5 min. with acetic anhydride (150 ml.) and sodium acetate (40 g.) and the solution poured into water (500 ml.) and kept until the practically pure *styrene* (46 g., 73%) solidified; recrystallization from light petroleum (b. p. 40—60°) raised the m. p. to 85—86° (Found: C, 45·7; H, 2·6. $C_8H_5FN_2O_4$ requires C, 45·3; H, 2·4%).

5-*Fluoroindole* (VII).—The styrene (VI) (20 g.), in a mixture of ethyl acetate (200 ml.) and glacial acetic acid (50 ml.), was hydrogenated in the presence of 10% palladium–charcoal at 40—50°/3 atm.; the theoretical quantity of hydrogen was absorbed within 10 min. The filtered solution was neutralized with solid sodium carbonate, filtered, and evaporated. 5-Fluoroindole (10·5 g., 83%) was best purified by steam distillation; it had m. p. 46—47°.

5-*Fluoro*-3-*indolylglyoxylyl Chloride*.—A solution of oxalyl chloride (17 ml.) in ether (60 ml.) was added with stirring and external cooling to 5-fluoroindole (13·5 g.) in ether (150 ml.). The yellow precipitate (19·0 g., 84%) was filtered off after 2 hr. and washed with a little ether. It could not be purified and was used directly for further experiments.

5-*Fluoro*-3-*indolylglyoxyl*-NN-*dimethylamide*. (II; R = Me).—A suspension of the chloride (9 g.) in ether (30 ml.) was slowly treated with dimethylamine (10 ml.) in ether. The *amide* (8·2 g., 88%) was collected, washed with water, and recrystallized from methanol; it formed

long needles, m. p. 201—202° (beginning to sublime) (Found: C, 61·8; H, 4·8; F, 8·1. $C_{12}H_{11}FN_2O_2$ requires C, 61·6; H, 4·7; F, 8·1%).

NN-*Diethyl-5-fluoro-3-indolylglyoxylamide* (II; R = Et) was prepared analogously in 82% yield; it formed needles, m. p. 208—210° (Found: C, 64·0; H, 5·9. $C_{14}H_{15}FN_2O_2$ requires C, 64·1; H, 5·8%).

5-*Fluoro*-NN-*dimethyltryptamine* (III; R = Me).—A solution of the glyoxylamide (II; R = Me) (7·0 g.) in tetrahydrofuran (150 ml.) was added dropwise to lithium aluminium hydride (8·5 g.) in ether (200 ml.). The mixture was refluxed with stirring for 1 hr., cautiously decomposed by successive addition of ethyl acetate and water, filtered, and concentrated. The residue was dissolved in ether, filtered, and treated with ethereal hydrogen chloride solution. The *hydrochloride* (2·8 g., 38%), crystallized from toluene–ethanol, had m. p. 175—176° (Found: C, 59·1; H, 6·9; F, 8·2. $C_{12}H_{16}ClFN_2$ requires C, 59·4; H, 6·6; F, 7·8). The picrate of the base melted at 180—181°.

NN-*Diethyl-5-fluorotryptamine* (III; R = Et).—The analogous treatment of the glyoxylamide (II; R = Et) (8·5 g.) in tetrahydrofuran (100 ml.) with lithium aluminium hydride (8·5 g.) in ether (200 ml.) gave the desired base (4·5 g., 59%) as a viscous oil, b. p. 160—165°/0·7 mm. In the crystallization of the *hydrochloride*, prepared as above, from toluene–ethanol, serious losses were sustained; the product had m. p. 192—193° (Found: C, 62·2; H, 7·6. $C_{14}H_{20}ClFN_2$ requires C, 62·1; H, 7·4%). The *picrate*, recrystallized from dilute ethanol, melted at 199—200° (Found: C, 51·9; H, 5·1. $C_{20}H_{22}FN_5O_7$ requires C, 51·8; H, 4·8%).

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## 1068. *The Mechanism of Solvolysis of γ-Phenyltetronic Acid Enol Esters. Part I. A Conductometric Study of the Methanolysis of γ-Phenyltetronic Acid Enol Benzoate.*

By (MRS.) ALICJA KIRKIEN-KONASIEWICZ and ALLAN MACCOLL.

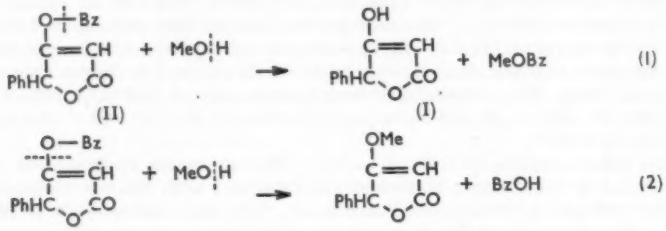
The methanolysis of γ-phenyltetronic acid enol benzoate under initially neutral or under basic conditions involves acyl–oxygen fission and is of the first order in ester. In the presence of pyridine and of its methyl derivatives, the first-order rate coefficients are linearly dependent on the concentration of base. The second-order rate constants obeyed the Brönsted relation, indicating general base catalysis.

γ-PHENYLTETRONIC ACID (I) is an αβ-unsaturated lactone. It has been shown that in the tautomeric equilibrium, the enol form (I) predominates in polar solvents. It is a stronger acid than acetic acid; its p$K_a$ in water is approximately the same (3·76) as that of unsubstituted tetronic acid.[1] The primary interest in γ-phenyltetronic acid enol esters (cf. II) is that they can be considered as a type of mixed anhydride. Characteristic of the solvolysis of acetic anhydride is the catalysis by bases, such as tertiary amines,[2,3] carboxylic anions,[4] nitrite ions,[5] hydroxyl ions,[6] and methoxide ions.[3] It was of interest to examine first the neutral methanolysis of γ-phenyltetronic acid enol benzoate, and then the effect of bases, with a view to establishing the mechanism of solvolysis.

*The Mode of Fission and the Products of Reaction.*—The mode of fission can be established by the Cohen and Schneider criterion,[7] by which the position of bond fission in solvolysis is proved directly by the nature of the products. Acyl–oxygen fission (I) would lead to

[1] Haynes and Plimmer, *Quart. Rev.*, 1960, 292.
[2] Gold and Jefferson, *J.*, 1953, 1409, 1416; Bafna and Gold, *J.*, 1953, 1406.
[3] Koskikallio, *Suomen Kem.*, 1959, **32**, *B*, 41.
[4] Kilpatrick, *J. Amer. Chem. Soc.*, 1928, **50**, 2891; 1930, **52**, 1410, 1418.
[5] Lees and Saville, *J.*, 1958, 2262.
[6] Koskikallio, *Ann. Acad. Sci. Fennicae*, 1954, **11**, *A*, 57.
[7] Cohen and Schneider, *J. Amer. Chem. Soc.*, 1941, **63**, 3382.

methyl benzoate and γ-phenyltetronic acid, whereas alkyl–oxygen fission (2) would yield *O*-methyl-γ-phenyltetronic acid and benzoic acid. It was found that acyl–oxygen fission occurs during methanolysis of the ester under both initially neutral and basic conditions, at 55° and 95°, the former being the temperature at which all the kinetic work was done. Thus an 18·1mM-solution of ester gave on titration (Thymol Blue–Methyl Red mixed




indicator at room temperature) the theoretical amount (99·5%) of γ-phenyltetronic acid. The methanol was removed from the titrated solution, and the residue extracted with ether. The oil recovered from the dried extract was hydrolysed with an excess of 0·1N-sodium hydroxide for 3 hours at 100°. From back-titration of the excess alkali it was found that the concentration of methyl benzoate was 17·5 mmoles $l.^{-1}$ (95·0%). Pure benzoic acid was recovered by acidification of the titrated solution. The methyl ether is stable to alkali and so the 95% of methyl benzoate and 99·5% of γ-phenyltetronic acid establishes acyl–oxygen fission on alkaline methanolysis.

The same procedure was adopted with runs under kinetic conditions, with a time of heating of the order of ten half-lives (see Table 1). These results and those given below show conclusively that under both initially neutral and initially basic conditions, acyl–oxygen fission occurs.

## Results

*Kinetics of the Neutral Methanolysis.*—Because of the methanolysis in the presence of alkali, direct titration could not be used for estimating the extent of reaction. Use was made of the solubilities of γ-phenyltetronic acid and its benzoate in water. To a methanolic solution (10 ml.) of γ-phenyltetronic acid and its benzoate, water (100 ml.) was added and the precipitated ester was filtered off. The filtrate was titrated with phenolphthalein as indicator. The precipitate was dissolved in methanol and titrated to the mixed indicator referred to above. Two experiments gave γ-phenyltetronic acid 98, 102%, and γ-phenyltetronic acid enol benzoate 107, 110%. This technique was then applied to a kinetic run at 55°. The results are shown in Table 2, concentrations being in mmole $l.^{-1}$. Analysis of these results by the first-order rate law gave $10^5 k_1 = 1{\cdot}91$ $sec.^{-1}$. There was no fall off in rate constant as the reaction proceeded.

The analytical method was not used in the comprehensive study, since it was tedious and not very accurate. As γ-phenyltetronic acid is a moderately strong acid, conductance was

Table 1.

Product analysis of reactions at 55°.

| Base | Time of heating (hr.) | MeOBz (%) | Acid * (%) | Base | Time of heating (hr.) | MeOBz (%) | Acid * (%) |
|---|---|---|---|---|---|---|---|
| None ..... | 100 | 98·5 | 92·5 | 2-Picoline ..... | 12 | — | 52·5 |
| | 1200 | 68·5 | 27·0 | | 21 | 106 | 36·3 |
| Pyridine ..... | 6 | 82 | — | 2,6-Lutidine ... | 6 | 88 | 106 |
| | 24 | 103 | 51·6 | 2,4,6-Collidine | 6 | 97·5 | 87·5 |
| | | | | 0·1N-NaOH ... | — | 95·0 | 99·5 |

* γ-Phenyltetronic acid.

TABLE 2.

The rate of neutral methanolysis at 55°.

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Time (hr.) | 3·05 | 4·00 | 6·10 | 8·00 | 10·70 | 15·00 | 23·50 |
| Concn. of ester | 27·4 | 29·6 | 27·9 | 23·4 | 18·6 | 12·9 | 7·9 |
| Concn. of ester (as acid) | — | 29·4 | 28·0 | 23·4 | 18·2 | 14·3 | 7·7 |

TABLE 3.

Increase of specific conductance of methanolic γ-phenyltetronic acid with time.

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Time (hr.) | 0 | 25·5 | 49 | 97 | 144 | 164 | 189 | 213 | 240 | 264 | 312 | 408 |
| $\lambda_s$ (μmho cm.$^{-1}$) | 17·8 | 18·2 | 18·8 | 20·2 | 20·8 | 21·4 | 22·1 | 22·6 | 23·0 | 23·7 | 24·3 | 26·3 |

measured instead. However, two difficulties occurred. First it was impossible to obtain reproducible calibration curves for γ-phenyltetronic acid in methanol, presumably because of traces of conducting impurity in the acid. Secondly, the specific conductance ($\lambda_s$) of methanolic solutions of the acid at 55° increases slowly with time (Table 3); the relation is approximately linear. This made $\lambda_s$ at the completion of methanolysis difficult to determine.

From conductance measurements on the ester undergoing methanolysis it is found that the change in $\lambda_s$ with time can be divided into two parts, the first fast, and the second slow (Fig. 1). The fast part lasts about a day, whereas the slow can be studied over weeks. The fast part is the neutral methanolysis of the ester; the slow part is due to some subsequent reaction of either or both of the products.

Arising from the initial attempts to obtain calibration curves of specific conductance against concentration of the acid it was found that the relation

$$c/\lambda_s = \alpha + \beta\lambda_s \quad (3)$$

was reasonably well obeyed, where α and β are constants and $c$ is the concentration of γ-phenyltetronic acid. The following iterative method was devised to determine α and β, based on a trial value of $k_1$, namely, $k_1^0$.

Now
$$d\lambda_s/dt = (d\lambda_s/dc)(dc/dt) \quad (4)$$

and
$$d\lambda_s/dc = (\alpha + 2\beta\lambda_s)^{-1} \quad (5)$$

$$dc/dt = k_1(c_\infty - c)$$
$$= k_1[\alpha(\lambda_s^\infty - \lambda_s) + \beta\{(\lambda_s^\infty)^2 - \lambda_s^2\}] \quad (6)$$

Hence substituting (5) and (6) in (4) gives:

$$d\lambda_s/dt = k_1[\alpha(\lambda_s^\infty - \lambda_s) + \beta\{(\lambda_s^\infty)^2 - \lambda_s^2\}]/(\alpha + 2\beta\lambda_s). \quad (7)$$

If $\lambda_s = 0$ when $t = 0$, then

$$(d\lambda_s/dt)_0 = (k_1/\alpha)[\alpha\lambda_s^\infty + \beta(\lambda_s^\infty)^2] \quad (8)$$
$$= k_1[1 + \omega\lambda_s^\infty]\lambda_s^\infty \quad (9)$$

where $\omega = \beta/\alpha$. If now the observed conductance at time $t$, $\lambda_s'$, is plotted against $t$ for the first 60 minutes, $\lambda_s^0$ and $(d\lambda_s/dt)_0$ may be obtained. In this way, $\lambda_s$ $(= \lambda_s' - \lambda_s^0)$ may be obtained as a function of time. Further, from a plot of $\lambda_s'$ against $t$ for the first 300 hours, $(\lambda_s^\infty)'$ may be obtained by extrapolation to zero time, the points for the first 60 hours being neglected. Thus $\lambda_s^\infty$ $[= (\lambda_s^\infty)' - \lambda_s^0]$ is obtained, and also a correction factor for the rate of change of the conductance of γ-phenyltetronic acid with time. The $\lambda_s$ values are then corrected for this effect. Next an estimate of $k_1^0$ is made and equation (9) solved for $\omega^0$. Superscripts 0, 1, 2, . . . refer to the zero, first, second . . . approximation. Equation (3) may be written as

$$c/\lambda_s = \alpha(1 + \omega\lambda_s) \quad (3')$$

and, when $c_\infty$ and $\lambda_s^\infty$ are known, it may be solved for $\alpha^0$. $\beta^0$ is then obtained from $\beta^0/\alpha^0 = \omega^0$. From the values of $\lambda_s$ at time $t$, $c$ can be obtained from equation (3) or (3′).

The next step is to calculate $k_1^1$ the second approximation from the $c$ values, and repeat the procedure with this value of $k_1$. This will lead to $\omega^1$, $\alpha^1$, and $\beta^1$, and hence to a new set of $c$

values and thus $k_1$[2]. The procedure may be repeated until successive values of $k_1$ do not differ by more than 2%. Three cycles are usually sufficient. Rate constants obtained in this fashion are shown in Table 4 and lead to the mean value $10^5k_1 = 2{\cdot}25$ sec.$^{-1}$, in reasonable agreement with the value obtained from the analytical method reported earlier.

The possibility of catalysis by the platinum electrodes was investigated by using a cell with wire electrodes. The cell constant was 0·671 cm.$^{-1}$ compared with the usual 0·03—0·06 cm.$^{-1}$.

TABLE 4.

$k_1$ for neutral methanolysis at 55°.

| $c_{ester}$ (mmole l.$^{-1}$) | 73·8 | 36·3 | 36·7 | 24·6 | 22·2 | 21·3 |
|---|---|---|---|---|---|---|
| $10^5k_1$ (sec.$^{-1}$) | 2·23 | 2·23 | 2·24 | 2·11 | 2·72 | 1·94 |

TABLE 5.

The lack of catalysis by platinum.

| Time (hr.) | 0 | 2 | 4 | 6 | 8 | 10 | 12 |
|---|---|---|---|---|---|---|---|
| $\Delta\lambda_s$ ($\mu$mho cm.$^{-1}$) | 0 | 3·61 | 5·29 | 6·52 | 7·54 | 8·33 | 9·00 |
| $\Delta\lambda_s$ ($\mu$mho cm.$^{-1}$) for wire electrode cell | 0 | 3·45 | 5·16 | 6·27 | 7·25 | 8·01 | 8·68 |

The results (Table 5) led to first-order rate constants of $2{\cdot}13 \times 10^{-5}$ sec.$^{-1}$ in each case and show that the electrode surface has no significant influence on the rate of reaction.

In assigning a mechanism to the reaction which has been shown to be of the first order in ester (Table 4) over the concentration range 20—70 mmole l.$^{-1}$, use is made of two general criteria. In the case of a bimolecular attack of the solvent molecule at the carbonyl centre of the ester, the rate of reaction would be affected by steric hindrance and subject to base catalysis.[8] The rate of initially neutral methanolysis of γ-phenyltetronic acid enol acetate is appreciably greater than that of the benzoate.[9] Again, methanolysis in the presence of 8·7 mmoles l.$^{-1}$ of sodium methoxide was found to be too fast to follow. The same was observed in the presence of 10 mmoles l.$^{-1}$ of piperidine. However, pyridine, 2-picoline, 2,6-lutidine, and 2,4,6-collidine were found to be of a convenient basic strength for their catalytic influence to be studied under the experimental conditions used for the neutral runs. This work is described in the next section, but, anticipating the results, it may be noted that the dependence of $k_1^B$ upon base is given by

$$k_1^B = k_1^N + k_2^B[B], \qquad (10)$$

and that $k_1^N$ is obtained in this fashion and agrees within the experimental error with that derived from the neutral runs.

Analysis of the concentration–time data for the neutral reaction shows that there is no fall-off in rate coefficient as the reaction proceeds. This eliminates the possibility that the methoxide ion is the attacking agent under initially neutral conditions, as the concentration of methoxide ions would be progressively reduced as the concentration of γ-phenyltetronic acid increases during reaction. The conclusion to be drawn from these experiments is that methanolysis proceeds by attack of methanol upon the ester, leading to first-order kinetics.

*Kinetics of the Base-catalysed Methanolysis.*—It was found that the conductance of γ-phenyltetronic acid in the presence of bases such as pyridine or its methyl derivatives is sufficiently high for traces of conducting impurities to be without noticeable effect, in contrast with the behaviour in the absence of base. Reproducible calibration curves were obtained for different samples of both acid and methanol. For fast reactions (in presence of high concentrations of base) $\lambda_s$ for a given concentration of ester calculated from the calibration curve was equal to the observed value after ten half-lives. Moreover, infinity values in terms of acid concentrations obtained by the Swinbourne method [10] were in fair agreement with those calculated on the basis of the weight of ester taken (Table 6). In view of this, rate constants in the presence of bases were evaluated by use of a calibration curve in which specific conductance is plotted against concentration of acid (Fig. 2). Along with the calibration points are points representing the infinity values for a number of runs. That all fit on a common line further justifies the use of calibration curves. Similar curves were obtained for 1-picoline, 2,6-lutidine, and 2,4,6-collidine. Methanolysis in all cases followed first-order kinetics, the constant $k_1^B$

[8] Ingold, "Structure and Mechanism in Organic Chemistry," Bell, London, 1953, pp. 400, 321.
[9] Konasiewicz, *J.*, 1961, following paper.
[10] Swinbourne, *J.*, 1960, 2371.

being obtained from a plot of log $(c_\infty - c_t)$ against time. The $c_t$ values were obtained from a smoothed curve of concentration values in turn obtained from the calibration curve. A typical plot is shown in Fig. 3. From each of the runs, $k_2^B$ was calculated from $k_2^B = (k_1^B - k_1^N)/[B]$, or from the slope of a plot of $k_1^B$ against [B]. The intercept gave $k_1^N$. Typical rate constants for reactions in methanol containing 51·7 mmoles l.$^{-1}$ of pyridine are shown in Table 7. The reaction is clearly of the first order. Two runs were done at an initial ester concentration of about 20 mmoles l.$^{-1}$, one in the wire electrode cell, the other in the presence of 19·0 mmoles l.$^{-1}$ of γ-phenyltetronic acid in methanol containing 200 mmoles l.$^{-1}$ of pyridine. The rate constants were $4·75 \times 10^{-4}$ and $4·51 \times 10^{-4}$ sec.$^{-1}$, to be compared with the mean of six determinations, namely, $4·49 \times 10^{-4}$ sec.$^{-1}$. Again there was no catalysis by platinum or inhibition by acid. The latter was also shown to be true for 2-picoline and collidine. The plots of $k_1^B$ against [B] for the four bases are shown in Fig. 4, the complete experimental results being recorded in the

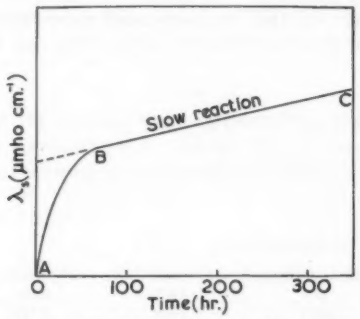



FIG. 1. Variation of conductance with time in the neutral methanolysis of γ-phenyltetronic acid enol benzoate.

The intercept give $A_s^\infty$. A—B = Methanolysis; B—C slow reaction.

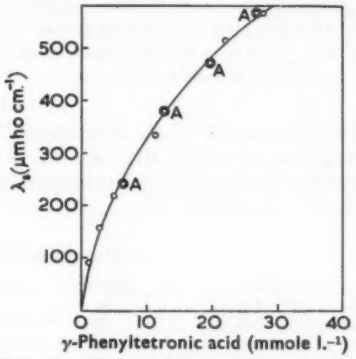



FIG. 2. The specific conductance of γ-phenyltetronic acid in methanol containing 200 mmoles l.$^{-1}$ of pyridine.

A = Infinity points from kinetic runs; others are calibration points.

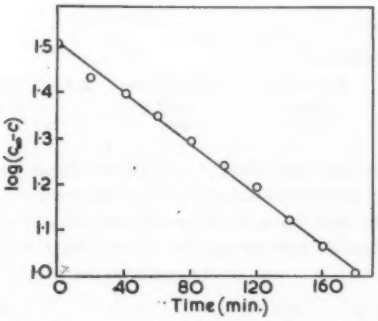



FIG. 3. A typical first-order log plot.

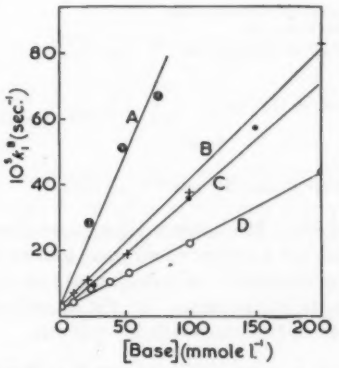



FIG. 4. The dependence of first-order rate constants on the concentration of base.

A, 2,4,6-Collidine. B, 2,6-Lutidine. C, 2-Picoline. D, Pyridine.

experimental section. For pyridine, values were calculated from $k_2^B = (k_1^B - k_1^N)/[B]$ with $k_1^N$ taken as $2{\cdot}23 \times 10^{-5}$ sec.$^{-1}$, as shown in Table 8; these gave a mean value of $k_2^B$ of $2{\cdot}15 \times 10^{-4}$ l. mmole$^{-1}$ sec.$^{-1}$ or $2{\cdot}15 \times 10^{-3}$ l. mmole$^{-1}$ sec.$^{-1}$. Values of $k_2^B$ for the other bases, together with p$K_b$ values in water are shown in Table 9.

Some runs were done in the presence of quinine (p$K_b$ 6·66). Good first-order behaviour was observed, but in base concentrations of 10 and 16·4 mmoles l.$^{-1}$, the mean values of $k_2^B$ were $5{\cdot}6 \times 10^{-2}$ and $10{\cdot}4 \times 10^{-2}$ l. mole$^{-1}$ sec.$^{-1}$, respectively. $k_1^B$ thus increases much more rapidly than [B]. This was thought to be associated with the diacidic character of the base, and the runs were not pursued further.

## Discussion

*The Mechanism of the Reaction.*—Base-catalysed methanolysis may involve (1) the nucleophilic attack of the base at the carbonyl centre, (2) specific base catalysis by methoxide ions formed by the interaction of the base with the solvent, or (3) general base

Table 6.

Infinity values of $\lambda_\infty$ (concns. in mmole l.$^{-1}$).

| Base | Pyridine | 2-Picoline | 2,6-Lutidine | 2,4,6-Collidine | Quinine |
|---|---|---|---|---|---|
| Concn. (wt. of ester) ..... | 19·2 | 10·8 | 9·7 | 18·7 | 9·08 |
| Concn. (Swinbourne)..... | 19·8 | 10·9 | 10·5 | 18·8 | 9·00 |

Table 7.

Rate constants for reaction in methanol containing 51·7 mmole l.$^{-1}$ of pyridine.

| Concn. of ester (mmole l.$^{-1}$) ..... | 12·8 | 14·1 | 21·9 | 27·5 | 36·8 | 38·8 | 42·8 |
|---|---|---|---|---|---|---|---|
| $10^5 k_1^B$ (sec.$^{-1}$) ..... | 13·1 | 13·2 | 13·3 | 12·7 | 13·1 | 12·7 | 13·7 |

Table 8.

Values of $k_2^B$ for B = pyridine.

| Concn. of base (mmole l.$^{-1}$) ..... | 10·1 | 24·4 | 39·5 | 51·7 | 100 | 200 |
|---|---|---|---|---|---|---|
| $10^5 k_1^B$ (sec.$^{-1}$) ..... | 4·39 | 8·50 | 10·1 | 13·1 | 22·2 | 44·9 |
| $10^4 k_2^B$ (l. mmole$^{-1}$ sec.$^{-1}$) ..... | 2·12 | 2·57 | 1·99 | 2·10 | 2·00 | 2·13 |

Table 9.

Catalytic rate constants.

| Base | Pyridine | 2-Picoline | 2,6-Lutidine | 2,4,6-Collidine |
|---|---|---|---|---|
| p$K_b$ ..... | 8·78 [11] | 8·04 [11] | 7·28 [11] | 6·55 [12] |
| $10^3 k_2^B$ (l. mmole$^{-1}$ sec.$^{-1}$) ..... | 2·15 | 3·29 | 3·89 | 10·2 |

catalysis. Mechanism (1) can be eliminated by the fact that α-methylpyridines should be subject to steric hindrance, and so the rate of methanolysis should be depressed. This is not observed; in fact the rate of methanolysis increases, though not linearly, with the strength of the base. In the second case, methoxide ions would be formed by the interaction of the base with the solvent

$$B + MeOH \rightleftharpoons BH^+ + MeO^- \qquad (11)$$

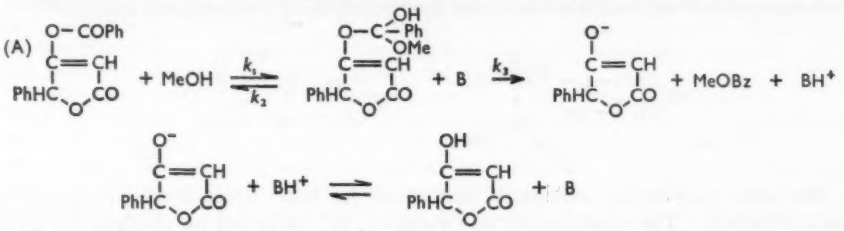
The methoxide ion concentration would thus be proportional to [B]/[BH$^+$] and consequently the rate of reaction would be directly proportional to the basic strength of the catalyst. This is not observed. Also the equilibrium (11) would be affected both by the acid formed during the reaction, and by initially added acid. γ-Phenyltetronic acid (TH) is a stronger acid than methanol:

$$TH + B \rightleftharpoons T^- + BH^+ \qquad (12)$$

and thus the equilibrium (12) would be of much greater importance than (11). Under these conditions the methoxide ion concentration would become proportional to [T$^-$]/[TH] and a decrease in rate, either as the reaction proceeds or in the presence of added acid,

[11] Andon, Cox, and Herrington, *Trans. Faraday Soc.*, 1954, **50**, 918.
[12] Golombic and Orchin, *J. Amer. Chem. Soc.*, 1957, **79**, 2365.

would be expected. Neither of these is observed, so mechanism (2) may be excluded. The methanolysis is thus unambiguously general-base catalysed.



Either a bimolecular or a termolecular mechanism is consistent with the observed facts. Thus the bimolecular mechanism may be written as (A) and, for $k_2 \gg k_3[B]$, the kinetic equation is

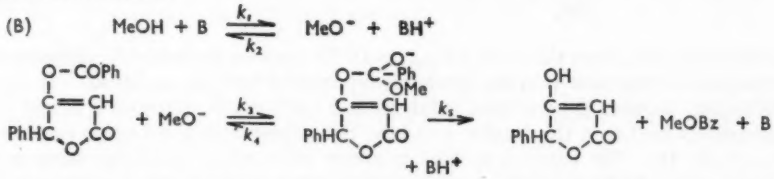
$$d[P]/dt = k_1k_3[A][B][S]/k_2, \quad (13)$$

where [P], [A], and [S] represent the concentrations of products, ester, and methanol, respectively. This implies a pre-equilibrium, with the attack of the base on the complex rate-determining. Scheme (B) would also give the same kinetic behaviour, namely:

$$d[P]/dt = K_bk_3k_5[A][B][S]/k_4, \quad (14)$$

where $K_b$ is the basic dissociation constant of the base B in methanol.

Alternatively a termolecular mechanism involving (C) or (D), namely synchronous attack by MeOH and B or by $MeO^-$ and $BH^+$, would give the same dependence of rate on reagent concentrations.



In the present work, a marked increase in rate constant ($k_2$) was observed as the basic strength of the catalyst increased, namely, collidine > lutidine > picoline > pyridine. This result, as has been shown, precludes the possibility of nucleophilic attack by the base, which *a priori* might have seemed the most probable mechanism. Preliminary results on γ-phenyltetronic acid enol acetate gave the $k_2$ sequence pyridine > collidine > lutidine > picoline, and it seems that in this case the smaller size of methyl than of phenyl permits nucleophilic attack.

Following Brönsted,[13] we write:

$$k_2^B = GK_b^\beta, \quad (15)$$

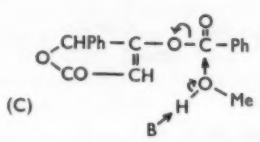
where $G$ is a constant and $K_b$ is the basic dissociation constant. Equation (15) may be written

$$\log k_2^B = \log G + \beta \log K_b = \log G - \beta.pK_b, \quad (16)$$

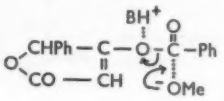
and hence a plot of $\log k_2^B$ against $pK_b$ should yield a straight line. A difficulty occurs in that, while the kinetics were investigated in absolute methanol, $pK_b$ values are obtainable only for aqueous solutions. However, Bell [14] has shown that for a series of similar bases $K_b(MeOH)/K_b(H_2O)$ is a constant, and expression (16) will still hold in these circumstances. There is also the temperature dependence of $K_b$ to consider. The plot is shown in Fig. 5, the slope of the line yielding the value 0·3 for β. Such a relation has

[13] Brönsted, *Chem. Rev.*, 1928, **5**, 322.
[14] Bell, "The Proton in Chemistry," Methuen, London, 1959, p. 44.

been found in a number of cases, such as the mutarotation of glucose in aqueous solution,[15] the decomposition of nitramide in isopentyl alcohol [16] and *m*-cresol,[17] the reaction of acetic anhydride [18] with certain bases, and the hydrolysis of *p*-nitrophenol acetate.[19]




(C)




(D)

The same mechanistic ambiguity that exists for base catalysis also exists for the neutral reaction. The second-order rate constant, $k_2^N$, obtained by dividing $k_1^N$ by the concentration of methanol, has the value $9{\cdot}8 \times 10^{-7}$ l. mole$^{-1}$ sec.$^{-1}$. This fits roughly

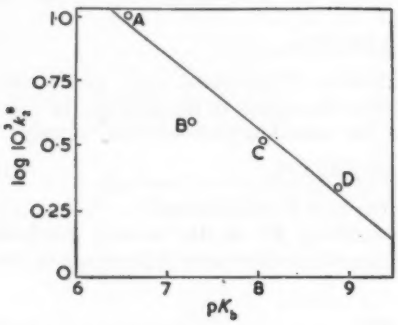



FIG. 5. The Brönsted relation between log $k_2^B$ and p$K_b$.

A, 2,4,6-Collidine. B, 2,6-Lutidine. C, 2-Picoline. D, Pyridine.

on the Brönsted plot, when the value p$K_{auto.} = 16{\cdot}7$ is used for methanol.[20] Thus methanol takes the place of the base B in the mechanism proposed for basic catalysis. In this case the distinction between general base catalysis and nucleophilic catalysis [21] is lost. Since all mechanisms lead to a third-order rate law, the appropriate third-order constants are listed in Table 10. The value of $k_3^{Py}/k_3^N$ is about 2000, which is of the same order of magnitude as that (1500) found by Koskikallio [3] for the methanolysis of acetic anhydride.

TABLE 10.

Third-order rate constants.

| Base | Methanol | Pyridine | 2-Picoline | 2,6-Lutidine | 2,4,6-Collidine |
|---|---|---|---|---|---|
| $10^5 k_3^B$ (l.$^2$ mole$^{-2}$ sec.$^{-1}$) ..... | 0·0041 | 9·0 | 14 | 16 | 43 |

## EXPERIMENTAL

*Preparation of Materials.*—Methanol was purified by distillation through a 3-ft. column packed with glass helices. The specific conductance was 0·3—0·4 μmho cm.$^{-1}$. γ-Phenyltetronic acid was obtained from *O*-acetylmandelyl chloride and diethyl malonate.[22] A typical sample had m. p. 127°.

γ-Phenyltetronic acid enol benzoate was prepared by either of the following methods. The acid (I), dissolved in 2N-sodium carbonate, was shaken with a slight excess of benzoyl chloride until the product crystallised. The latter was suspended in an ice-cold solution of sodium hydrogen carbonate, filtered off, and twice recrystallised from light petroleum (b. p. 60—80°).[23]

[15] Brönsted and Guggenheim, *J. Amer. Chem. Soc.*, 1927, **49**, 2554.
[16] Brönsted and Vance, *Z. phys. Chem.*, 1933, *A*, **163**, 240.
[17] Brönsted, Nicholson, and Delbanco, *Z. phys. Chem.*, 1934, *A*, **169**, 379.
[18] Gold and Jefferson, *J.*, 1953, 1409.
[19] Jencks and Carriuolo, *J. Amer. Chem. Soc.*, 1960, **82**, 1778.
[20] Hammett, " Physical Organic Chemistry," McGraw-Hill, New York, 1940, p. 256.
[21] Bender, *Chem. Rev.*, 1960, **60**, 53.
[22] Haynes, Plimmer, and Stanners, *J.*, 1956, 4661.
[23] Jamieson, Ph.D. Thesis, Edinburgh, 1959.

Alternatively the acid was treated in cooled pyridine with an excess of benzoyl chloride. The solid was filtered off, washed with dilute hydrochloric acid and ice-cold sodium hydrogen carbonate solutions until free from pyridine and acid, then recrystallised as above. A typical specimen had m. p. 110° (Found: C, 72·9; H, 4·4. Calc. for $C_{17}H_{12}O_4$: C, 72·9; H, 4·3%) and no more than 0·6% of non-acid impurities as determined by titration of a methanolic solution with alkali, Thymol Blue–Cresol Red being used as indicator.

Pyridine was purified *via* the zinc chloride salt,[24] and other bases by distillation.

*Kinetic Methods.*—The conductance cells were of a conventional type with bright platinum electrodes. The cells used for most runs had constants in the range 0·03—0·06 cm.$^{-1}$; a cell with platinum wire electrodes had a cell constant of 0·671 cm.$^{-1}$. Conductance measurements were done with an a.c. bridge, the accuracy being about ±0·2%. The thermostat temperature was 54·95° ± 0·01°. All basic solutions were made up volumetrically, by dissolving a given weight, in methanol. Solutions for the kinetic runs were prepared by dissolving a known weight of ester in 25 ml. of solvent that had been heated to 55°. The conductance cell was then filled by means of a pipette and $\lambda_s$ was measured at intervals. From the appropriate calibration curve, in the case of the base-catalysed reaction, concentration was obtained as a function of time, and rate constants were calculated from the first-order law.

*Kinetic Results.*—The results are tabulated here (concentrations in mmole l.$^{-1}$).

*Base*: *Pyridine.*

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| [Base] | 1·00[a] | ← | 10·1 | → | | ← | 24·4 | → | | | |
| [Ester] | 36·1 | 15·1 | 16·9 | 22·4 | 32·1 | 15·7 | 20·8 | 21·7 | 21·6 | 21·7 | |
| $10^5k_1$ (sec.$^{-1}$) | 2·38 | 4·25 | 4·58 | 4·42 | 4·30 | 8·31 | 8·13 | 8·39 | 8·85 | 8·82 | |
| $10^5k_1$ (sec.$^{-1}$) (mean) | 2·38 | | | 4·39 | | | | 8·50 | | | |
| [Base] | ← | 39·5 | → | | | ← | 51·7 | → | | | |
| [Ester] | 16·8 | 17·7 | 22·4 | 32·9 | 12·8 | 14·1 | 21·9 | 27·5 | 36·8 | 38·8 | 42·8 |
| $10^5k_1$ (sec.$^{-1}$) | 9·98 | 9·44 | 10·70 | 10·30 | 13·1 | 13·2 | 13·3 | 12·7 | 13·1 | 12·7 | 13·7 |
| $10^5k_1$ (sec.$^{-1}$) (mean) | | 10·1· | | | | | | 13·1 | | | |
| [Base] | ← | 100 | → | | ← | 200 | → | | | | |
| [Ester] | 15·8 | 18·1 | 45·5 | 13·1 | 20·0 | 26·5 | 36·0 | 20·0[b] | 20·9[c] | | |
| $10^5k_1$ (sec.$^{-1}$) | 22·1 | 22·6 | 21·9 | 44·5 | 46·2 | 44·0 | 42·0 | 47·5 | 45·1 | | |
| $10^5k_1$ (sec.$^{-1}$) (mean) | | 22·2 | | | | | 44·9 | | | | |

*Base*: *2-Picoline.*

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| [Base] | ← | 25 | → | ← | 100 | → | | ← | 150 → |
| [Ester] | 7·80 | 14·8 | 7·33 | 13·10 | 19·00 | 18·6[d] | 23·1[e] | 10·8 | 21·7 |
| $10^5k_1$ (sec.$^{-1}$) | 8·74 | 8·64 | 35·8 | 34·5 | 37·5 | 34·1 | 38·3 | 57·6 | 57·9 |
| $10^5k_1$ (sec.$^{-1}$) (mean) | | 8·69 | | | 36·0 | | | | 57·8 |

*Base*: *2,6-Lutidine.*

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| [Base] | ← | 10·0 | → | ← | 20·0 | → | ← | 50 | → |
| [Ester] | 4·88 | 7·83 | 9·70 | 6·69 | 7·74 | 13·7 | 12·8 | 18·8 | 20·9 |
| $10^5k_1$ (sec.$^{-1}$) | 6·87 | 6·90 | 6·85 | 10·7 | 9·60 | 10·4 | 18·8 | 18·6 | 18·4 |
| $10^5k_1$ (sec.$^{-1}$) (mean) | | 6·87 | | | 10·2 | | | 18·6 | |
| [Base] | ← | 100 | → | ← | 200 | → | | | |
| [Ester] | 12·6 | 16·3 | 37·6 | 10·0 | 10·3 | 43·9 | | | |
| $10^5k_1$ (sec.$^{-1}$) | 37·3 | 36·8 | 36·6 | 82·1 | 83·0 | 84·5 | | | |
| $10^5k_1$ (sec.$^{-1}$) (mean) | | 36·9 | | | 83·2 | | | | |

*Base*: *2,4,6-Collidine.*

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| [Base] | ← | 23·7 | → | ← | 50·0 | → | ← | 75 | → |
| [Ester] | 6·99 | 10·7 | 13·7 | 8·1 | 11·6 | 9·13 | 9·71 | 18·7 | 35·0 |
| $10^5k_1$ (sec.$^{-1}$) | 28·3 | 28·6 | 28·1 | 55·8 | 56·3 | 55·8 | 65·8 | 66·0 | 70·5 |
| $10^5k_1$ (sec.$^{-1}$) (mean) | | 28·3 | | | 55·9 | | | 67·4 | |

[a] Rate calculated as for neutral reaction. [b] 19·0 mmoles l.$^{-1}$ γ-phenyltetronic acid initially added. [c] In cell with wire electrodes. [d] 9·13 mmoles l.$^{-1}$ of γ-phenyltetronic acid initially added. [e] 13·8 mmoles l.$^{-1}$ of γ-phenyltetronic acid initially added. [f] 8·1 mmoles l.$^{-1}$ of γ-phenyltetronic acid initially added.

The authors thank Professor L. J. Haynes for suggesting the problem and for continued encouragement; Dr. C. A. Bunton for many helpful discussions; and Messrs. Chin and McGregor for assistance with some of the experimental work.

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[*Received, May 24th*, 1961.]

[24] Vogel, " Practical Organic Chemistry," Longmans, London, 1948, p. 175.

## 1069. *The Solvolysis of γ-Phenyltetronic Acid Enol Esters. Part II.* The Methanolysis of γ-Phenyltetronic Acid Enol Acetate.*

By (Mrs.) Alicja M. Kirkien-Konasiewicz.

Methanolysis of γ-phenyltetronic acid enol acetate under basic conditions is shown to follow a second-order rate law, the rate being proportional to the concentration of ester and to the concentration of base. By using a series of methyl-substituted pyridines of different basic strengths, it is shown that the rate is determined by a balance between the basic strength and the steric hindrance of the methyl groups. This is in marked contrast to the behaviour of the benzoate, for which the basic strength was the sole factor determining the catalytic activity. It is concluded that, in the present case, the rate-determining step is the attack by the base on the neutral molecule. The catalysed methanolysis is thus an example of nucleophilic catalysis.

In Part I * it has been shown that γ-phenyltetronic acid enol benzoate undergoes methanolysis either by a bimolecular mechanism, following a pre-equilibrium, or by a termolecular mechanism, involving ester, solvent, and base or solvent, depending on whether it is studied under initially basic or initially neutral conditions. As the phenyl group in the benzoate causes a certain degree of crowding, it was thought of interest to study the acetate, for which steric considerations might be expected to be less important.

The nature of the products was established as described in Part I. For neutral methanolysis, after ~6 hours' heating at 55° 97% of γ-phenyltetronic acid and 93·4% of methyl acetate were recovered, indicating acyl–oxygen fission. In the presence of bases, product separation yielded the results shown in Table 1. Thus under both initially neutral and initially basic conditions, acyl–oxygen fission occurs.

Table 1.

Product analysis: reaction at 55°.

| Base | Heating (hr.) | MeOAc (%) | Acid (%) |
|---|---|---|---|
| None | 6 | 93·4 | 97 |
| Pyridine | 2 | — | 95 |
| 2,6-Lutidine | 3 | 104 | 113 |

*The Kinetics of Neutral Methanolysis.*—Neutral methanolysis was studied by the conductance technique and the results were analysed as described in Part I. Because methanolysis of the acetate is about six times faster than that of the benzoate at 55° (at which all kinetic runs were done), extrapolation for $\lambda_s^\circ$ and $(d\lambda_s/dt)_0$ was carried out over the first ten minutes of each run. The first-order rate coefficients obtained (Table 2) are

Table 2.

Rate coefficients for neutral methanolysis at 55°.

| Concn. (mmoles l.$^{-1}$) | 64·7 | 48·0 | 19·3 |
|---|---|---|---|
| $10^4 k_1$ (sec.$^{-1}$) | 1·46 | 1·44 | 1·48 |

independent of the initial concentration of ester. The methanolysis is thus of the first order, the mean rate constant being $1{\cdot}46 \times 10^{-4}$ sec.$^{-1}$. Comparing this value with that reported in Part I for γ-phenyltetronic acid enol benzoate, namely, $2{\cdot}25 \times 10^{-5}$ sec.$^{-1}$, gives the rate ratio acetate : benzoate as 6·5 : 1. This value is close to that (10 : 1) found for ethyl acetate and ethyl benzoate in alkaline hydrolysis, which proceeds by the $B_{Ac}2$ mechanism.[1] In both cases, the results can be attributed to the steric effect of the relatively bulky phenyl group. Specific base-catalysis by the methoxide ion is eliminated

* Part I, preceding paper.

[1] Ingold, " Structure and Mechanism in Organic Chemistry," Bell, London, 1953.

as a possible mechanism by the fact that the γ-phenyltetronic acid formed in the reaction does not cause a fall in the rate coefficient. The mechanism thus involves the attack of solvent upon the ester, as for the benzoate.

*The Kinetics of Base-catalysed Methanolysis.*—In the presence of 0·1N-sodium hydroxide, apparently instantaneous methanolysis took place. As with the benzoate, pyridine and its methyl derivatives, 2-picoline, 2,6-lutidine and 2,4,6-collidine proved to be of convenient strength for studying the catalysed reaction. In the presence of these bases, reproducible calibration curves of the concentration of γ-phenyltetronic acid against specific conductance of the solution were obtained. Use of these curves enabled the γ-phenyltetronic acid in a solution undergoing methanolysis to be determined at various stages of the reaction. A typical first-order plot [log $(c_\infty - c)$ against time] is shown in Fig. 1. The points all lie close to the line up to about 75% reaction. Observed infinity

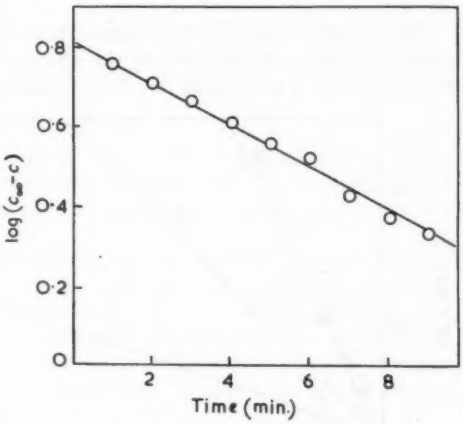



FIG. 1. A typical kinetic run in presence of 100 mmoles of 2,6-lutidine per l.

values of the concentration of γ-phenyltetronic acid (in mmoles $l.^{-1}$), together with those obtained by the Swinbourne method [2] and those from the weight of ester taken for the run (theor.), are shown in Table 3. By using a conductance cell with platinum wire electrodes

TABLE 3.

Infinity values for base-catalysed methanolysis obtained by various methods.

| Base | Obs. | Swinbourne | Theor. | $10^4k_1$ (sec.$^{-1}$) |
|---|---|---|---|---|
| Pyridine | 13·1 | 13·8 | 13·1 | 17·4 |
| α-Picoline | 10·7 | 10·7 | 11·2 | 4·2 |
| 2,6-Lutidine | 6·9 | 6·9 | 7·9 | 7·3 |

of cell constant 0·671 cm.$^{-1}$ (to be compared with values of 0·03—0·06 cm.$^{-1}$ for the cells normally used), it was shown that there was no surface catalysis by platinum. The rate constants were $6{\cdot}10 \times 10^{-4}$ and $5{\cdot}56 \times 10^{-4}$ sec.$^{-1}$, for the platinum wire and normal cells, respectively, for runs in methanol containing 10 mmoles of pyridine per l. A run in the presence of lutidine and γ-phenyltetronic acid (10 and 9·4 mmoles $l.^{-1}$, respectively) gave for the first-order rate constant $3{\cdot}96 \times 10^{-4}$ sec.$^{-1}$, to be compared with a mean value of $3{\cdot}77 \times 10^{-4}$ sec.$^{-1}$ in the absence of the acid.

The observed first-order rate coefficients ($k_1^B$) were proportional to the concentration of added base (Fig. 2). Thus, $k_1^B = k_1^N + k_2^B[B]$, where $k_1^N$ is the observed first-order rate constant for the neutral reaction, and $k_2^B$ is the catalytic constant. Values of the catalytic constants are shown in Table 4. It will be observed that the value of $k_1^N$

[2] Swinbourne, *J.*, 1960, 2371.

obtained from these experiments, is consistent with the value obtained from the independent study of the neutral reactions.

It is obvious (Table 4) that the Brönsted relation, $\log k_2^B = \alpha + \beta \log K_B$, is not followed in the case of the acetate, as it is in that of the benzoate.

TABLE 4.

The catalytic constants.

| Base | $10^3 k_2$ (mole$^{-1}$ l. sec.$^{-1}$) | p$K_B$ |
|---|---|---|
| Pyridine | 4·45 | 8·78 * |
| 2-Picoline | 0·75 | 8·04 * |
| 2,6-Lutidine | 2·08 | 7·28 * |
| 2,4,6-Collidine | 3·97 | 6·55 † |

* Andon, Cox, and Herrington, *Trans. Faraday Soc.*, 1954, **50**, 918.
† Golombic and Orchin, *J. Amer. Chem. Soc.*, 1957, **79**, 2365.

*Discussion.*—The rate of the base-catalysed methanolysis of γ-phenyltetronic acid enol acetate is extremely sensitive to the steric properties of the tertiary amines, as can be seen from Fig. 2 and Table 4. 2,4,6-Collidine, the strongest of the bases (p$K_B$ 6·55 in

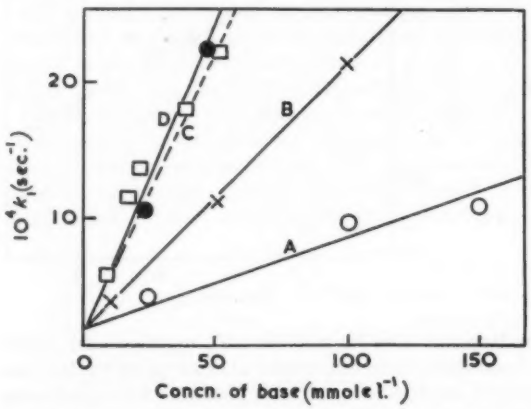
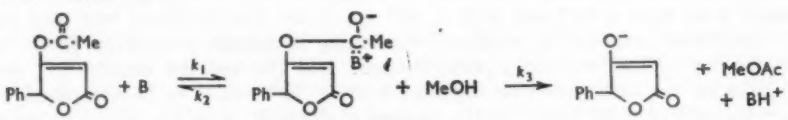



FIG. 2. Methanolysis of γ-phenyltetronic acid in presence of tertiary amines.

○, α-Picoline; ×, 2,6-lutidine; ●, 2,4,6-collidine, □, pyridine.

water), gives a second-order rate constant of $4·0 \times 10^{-2}$ mole$^{-1}$ l. sec.$^{-1}$, which is lower than that for pyridine, $4·5 \times 10^{-2}$ mole$^{-1}$ l. sec.$^{-1}$, in which the nitrogen atom is not sterically hindered. Also 2,6-lutidine, of basic strength appreciably higher than pyridine, actually has a much lower catalytic constant, only half that of pyridine; and α-picoline, although less sterically hindered than 2,6-lutidine, is a much weaker base, which explains its very low catalytic constant.

Mechanistically these results can be interpreted as a bimolecular nucleophilic attack of the base on the carbonyl centre, followed by the interaction of the complex so formed with the solvent:




This scheme would lead to the kinetic equation

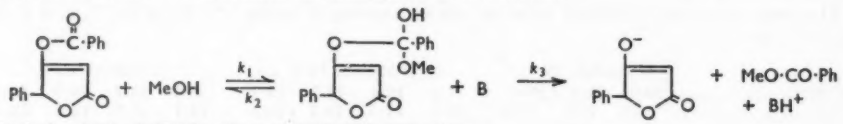
$$\frac{d[P]}{dt} = \frac{k_1 k_3 [A][B][S]}{k_2 + k_3[S]}$$

which for $k_3[S] \gg k_2$, reduces to

$$d[P]/dt = k_1[A][B],$$

where *P* stands for products, B is base, and A is ester. Nucleophilic attack is thus the rate-determining step and is followed by the rapid attack of the solvent on the complex, giving acyl–oxygen fission and the observed products, γ-phenyltetronic acid and methyl acetate. This scheme would predict a first-order disappearance of ester, since the concentration of base remains constant.

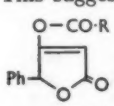
This behaviour contrasts strongly with that observed for γ-phenyltetronic acid enol benzoate. For in that case the Brönsted relation was obeyed and the kinetic behaviour was shown to be consistent with either a pre-equilibrium of solvent and ester, followed by the slow decomposition of the complex, or a termolecular mechanism, involving ester, base, and solvent. The former mechanism was written as:




which for $k_2 \gg k_3[B]$ leads to the kinetic equation

$$d[P]/dt = k_1k_3[A][B][S]/k_2.$$

This suggests a critical steric effect of the group R in the ester (A) which, if too large, precludes the possibility of nucleophilic catalysis, even in the presence of unsubstituted pyridine, thus forcing either a prior or a simultaneous attack by the solvent molecule.



(A)

Gold and his co-workers [3] studied the hydrolysis of acetic anhydride in the presence of a series of tertiary amines. 2-Methyl- or 2,6-dimethyl-pyridine showed a kinetic steric effect, while non-sterically hindered tertiary bases at low concentration obeyed the Brönsted law, the value of β being about 0·9. These results were interpreted in terms of the rate-determining transfer of the acetyl ion $Ac^+$ from the anhydride to the catalyst, followed by rapid hydrolysis of the resulting cation.* The same was shown to be true in the case of acetic formic anhydride.

Koskillalio [4] studied the methanolysis of acetic anhydride in the presence of pyridine. The catalytic effect of pyridine was not greatly different from that of acetate ions. Changing the solvent to water gives a $10^5$-fold increase in rate, pointing to a highly polar transition state. This suggested that the rate-determining step was addition of the catalyst to the anhydride molecule, a mechanism similar to that suggested for γ-phenyltetronic acid enol acetate. The rate constants for attack by pyridine and by methanol were $6{\cdot}5 \times 10^{-7}$ and $9{\cdot}9 \times 10^{-4}$ mole$^{-2}$ l. sec.$^{-1}$, giving a ratio ~1500. The corresponding ratio in the case of γ-phenyltetronic acid enol acetate was 7400.

## Experimental

γ-Phenyltetronic acid was prepared from *O*-acetylmandeloyl chloride and diethyl malonate.[5] A typical sample had m. p. 127°. The acetate was prepared by treating γ-phenyltetronic acid with an excess of acetic anhydride in the presence of a few drops of concentrated sulphuric acid; the solution was then diluted with chloroform and washed with ice-cold aqueous sodium hydrogen carbonate; the chloroform layer was dried ($Na_2SO_4$) and evaporated under reduced pressure; the oily brown residue crystallised and was recrystallised from light petroleum (b. p. 60—80°), having m. p. 79° (Found: C, 65·9; H, 4·65. Calc. for $C_{12}H_{10}O_4$: C, 66·1; H, 4·6%). Equivalent-weight determination, by titration of a methanolic solution with Thymol Blue–Cresol Red as indicator showed > 0·8% of non-acid impurities.

Pyridine was purified by recrystallisation of its zinc chloride salt; [6] other bases were distilled.

* Bunton *et al* (*Tetrahedron Letters*, 1961, 458) have shown by isotopic studies that the rate-determining step is the hydrolysis of acylpyridinium ions (cf. Butler and Gold, *Proc. Chem. Soc.*, 1960, 15).

[3] Gold and Bafra, *J.*, 1953, 1406; Gold and Jefferson, *J.*, 1953, 1409, 1416.
[4] Koskillalio, *Suomen Kem.*, 1959, **32**, *B*, 41.
[5] Haynes, Plimmer, and Stanners, *J.*, 1956, 4661.
[6] Vogel, "Practical Organic Chemistry," Longmans, Green & Co., London, 1948.

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The conductance cells used were of conventional design, with bright platinum electrodes and all had constants in the range 0·03—0·06 cm.$^{-1}$. The conductance measurements were done with a Pye bridge, the accuracy of the readings being $\pm 0{\cdot}2\%$. The thermostat temperature was 54·95° $\pm$ 0·01°.

The solutions of bases were prepared by weighing the base and making up the solution to a standard volume. The solutions of ester were made up by adding a known weight of ester to the pre-heated solvent. The solution was then added to the pre-heated conductance cell, and readings of $\lambda_s$ were made at the appropriate times. Points observed for the first few minutes were neglected, to allow for the attainment of thermal equilibrium. From the appropriate calibration curve, the concentration of $\gamma$-phenyltetronic acid was found as a function of time, and first-order rate constants were calculated in the conventional manner.

The rate constants tabulated refer to concentrations in moles l.$^{-1}$, $k_1$ in sec.$^{-1}$, and $k_2$ in mmole$^{-1}$ l. sec.$^{-1}$.

| | [Pyridine] 10·1 | | | [Pyridine] 19·7 | | | | [Pyridine] 24·4 | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| [Ester] | 20·0 | 21·5 | 29·6 | 11·3 | 12·4 | 16·7 | 22·7 | 8·3 | 18·7 | 20·0 | 26·3 |
| $10^4k_1$ | 5·38 | 5·56 | 5·75 | 10·8 | 11·5 | 10·3 | 10·3 | 14·1 | 13·1 | 13·5 | 13·0 |
| $10^5k_2$ | | 4·05 | | | 4·69 | | | | 4·90 | | |

| | [Pyridine] 39·5 | | | | [Pyridine] 57·7 | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| [Ester] | 10·3 | 13·8 | 16·0 | 22·3 | 10·7 | 11·2 | 14·6 | 16·0 | 26·5 | 36·6 |
| $10^4k_1$ | 17·4 | 18·4 | 17·4 | 18·0 | 23·0 | 26·0 | 21·6 | 19·3 | 19·3 | 23·0 |
| $10^5k_2$ | | 4·15 | | | | | 3·97 | | | |

| [α-Picoline] | 25·0 | | 100 | 150 | [2,4,6-Collidine] | 24·5 | 49·0 |
|---|---|---|---|---|---|---|---|
| [Ester] | 7·7 | 11·2 | 7·48 | 7·2 | [Ester] | 73·8 | 8·39 |
| $10^4k_1$ | 3·64 | 4·21 | 9·60 | 10·2 | $10^4k_1$ | 10·5 | 22·3 |
| $10^5k_2$ | 0·87 | | 0·81 | 0·58 | $10^5k_2$ | 3·70 | 4·25 |

| [2,6-Lutidine] | 10·0 | | | | 50 | | | 100 |
|---|---|---|---|---|---|---|---|---|
| [Ester] | 9·58 | 12·6 | 14·4 * | 23·1 | 6·46 | 8·64 | 10·0 | 7·53 |
| $10^4k_1$ | 3·26 | 3·62 | 3·96 | 4·25 | 10·4 | 11·0 | 11·1 | 21·2 |
| $10^5k_2$ | | 2·31 | | | | 1·87 | | 1·97 |

* In presence of 9·4 mmoles of $\gamma$-phenyltetronic acid per l.

The author thanks Dr. Allan Maccoll for friendly criticism and constant encouragement, Professor L. J. Haynes for suggesting the investigation of tetronic acid enol esters, and Dr. C. A. Bunton for helpful discussions.

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## 1070. *Studies in Hydrogen-bond Formation. Part X.* Complex-formation between a Variety of Organic Solutes in Carbon Tetrachloride.*

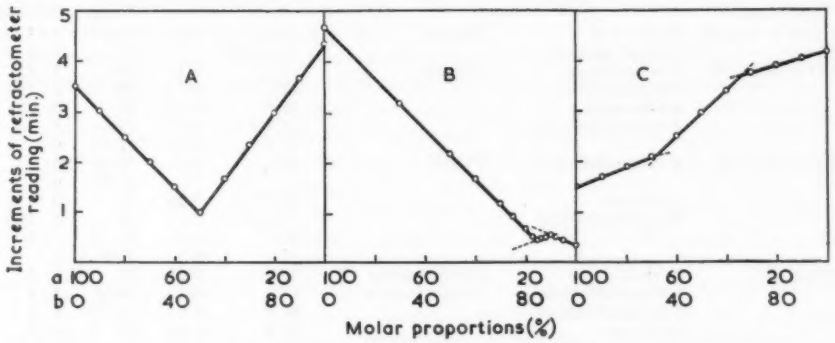
By C. H. GILES, R. B. MCKAY, and (in part) W. GOOD.

A number of pairs of solutes have been tested by the refractometric method in a non-bonding solvent, carbon tetrachloride. Intermolecular hydrogen-bonding of OH···O, CH···Cl, CH···N, OH···Cl, and ArOH···ArH types have been detected. The results agree with those obtained previously in hydrogen-bonding solvents, *e.g.*, benzene, dioxan, ethanol, water, and confirm the value of the method for measuring complex ratios in either bonding or non-bonding solvents. The theoretical basis of the linearity of the curves is discussed.

THE method of " continuous variations " with refractive index measurements is used in this work to measure the combining ratio of a variety of hydrogen-bonding organic solutes. Several hundred systems have been examined, and the complex ratios found, or

* Part IX, Giles and Nakhwa, *J. Appl. Chem.*, 1961, **11**, 197.

the reactivity of individual types of group, have in many cases been confirmed by other methods.[1-4] There are numerous cross-checks in the data, *e.g.*, the number of molecules of a solute B combined with a solute A agrees with the number of free bonding centres in A.




Relation between refractive index (as instrument reading) and ratio of components in carbon tetrachloride solution.

A: a, Chlorobenzene; b, phenol; 0·1M; 14·85°.
B: a, Hexachlorobenzene; b, phenol; 0·05M; 12·08°.
C: a, Benzene; b, phenol; 0·1M; 17·00°.

The method has also been used to detect intramolecular bonding, *e.g.*, in diols,[2] for which confirmation by infrared spectroscopy is available (ref. 5, p. 97). A recent comment on the method (ref. 5, p. 55) is that large numbers of the systems used here were examined in hydrogen-bonding solvents, *e.g.*, ethanol, benzene, and especially water, and that more positive value could be placed on the method if the only possibility for hydrogen bonding were between the two solutes. The present paper describes the application of this suggestion. It should, however, be emphasised that hydrogen bonding in aqueous solution is of the greatest importance in all biological systems and in many technical processes, and that in our view one of the principal advantages of this method is that it is almost the only simple one that can be used to study hydrogen-bonding combining ratios in dilute aqueous solution. Thus, of nearly thirty methods described by Pimentel and McClellan [5] only about ten can be used with aqueous media, and few if any are as widely applicable as the present.

The method of continuous variations has also been used successfully to determine combining ratios between metals and a chelating organic solute.[6]

In this paper we describe tests in carbon tetrachloride solution with a variety of pairs of solutes, chosen to represent the most important types of intermolecular bond, within the limits imposed by the small range of compounds that are sufficiently soluble in this solvent. The results are shown in the Figure and Table 1 which includes the results with this solvent reported previously. All relevant comparisons with systems in water or other bonding solvents are also shown.

[1] Arshid, Giles, McLure, Ogilvie, and Rose, *J.*, 1955, 67.
[2] (*a*) Arshid, Giles, Jain, and Hassan, *J.*, 1956, 72; (*b*) Arshid, Giles, and Jain, *J.*, 1956, 559, 1272.
[3] See, *e.g.*, Giles and Neustädter, *J.*, 1952, 3806; Allingham, Giles, and Neustädter, *Discuss. Faraday Soc.*, 1954, **16**, 92; Cameron, Giles, and MacEwan, *J.*, 1957, 4304; Giles and MacEwan, *J.*, 1959, 1791.
[4] Giles, in "Hydrogen Bonding," ed. Hadzi, Pergamon Press, London, 1959.
[5] Pimentel and McClellan, "The Hydrogen Bond," W. H. Freeman & Co., San Francisco, 1960.
[6] See, *e.g.*, Job and his collaborators, *Compt. rend.*, 1925—1935, **180—200**; Vosburgh and Cooper, *J. Amer. Chem. Soc.*, 1941, **63**, 437; and other papers quoted in ref. 2*a*.

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TABLE 1.

Comparison of results of complex-detection tests in carbon tetrachloride with those in bonding solvents.

| Type of bond | Solutes | | Solv.* | Total mol. concn. | Temp. | Mol. ratio of complex |
|---|---|---|---|---|---|---|
| Alk–OH + Ar–OH | Butan-1-ol | Phenol | $CCl_4$ | 0·1 | 15·85° | 1 : 1 |
| | Several alcohols | | T, D, W | | | 1 : 1 |
| –CHO + Alk–OH | Acetaldehyde | Ethanol | $CCl_4$ | 0·1 | 20 | 1 : 1 |
| | Benzaldehyde | | $CCl_4$ | 0·1 | 20 | 1 : 1 |
| | D-Glucose | | W [25] | 0·25 | 20 | 0 |
| | Propionaldehyde | | $CCl_4$ [25] | 0·2 | 17·5 | 1 : 1 |
| | | | W [25] | 0·2 | 17·5 | 0 |
| –CHO + Ar–OH | n-Butyraldehyde | Phenol | $CCl_4$ | 0·1 | 13·08 | 0 |
| | | | | | 17·00 | 0 |
| | D-Glucose | | W [25] | 0·25 | 20 | 0 |
| | Propionaldehyde | | $CCl_4$ [25] | 0·1 | 17 | 1 : 1(?) |
| | | | EG | 0·2 | 18 | 1 : 1 |
| | | | W | 0·2 | 17·5 | 0 |
| –CHO + N< | Acetaldehyde | Diethylamine | W [25] | 0·25 | 20 | 1 : 1 |
| | n-Butyraldehyde | Triethylamine | $CCl_4$ | 0·1 | 13·08 | 1 : 1 |
| | Formaldehyde | | W [25] | 0·2 | 20 | 1 : 1 |
| | D-Glucose | | W [25] | 0·25 | 20 | 1 : 1 |
| | Propionaldehyde | Dimethylformamide | $CCl_4$ [25] | 0·2 | 18 | 1 : 1 |
| | | | W [25] | 0·2 | 18 | 1 : 1 |
| | Terephthaldehyde | Triethylamine | T [25] | 0·2 | 18 | 1 : 2 |
| | Terephthaldehyde | | W [25] | 0·1 | 17 | 1 : 2 |
| >C=O + Alk–OH | Acetone | Methanol | C [25] | 0·1 | 20 | 1 : 2 |
| | | | D [25] | 0·1 | 20 | 1 : 2 |
| >C=O + Ar–OH | Acetone | Phenol | W [25] | 0·1 | 20 | 0 |
| | Di-isobutyl ketone | | D [25] | 0·25 | 20 | 1 : 2 |
| | Ethyl methyl ketone | | $CCl_4$ | 0·1 | 14·83 | 1 : 1, 1 : 2 |
| Ar–H + ArOH | Benzene | Phenol | $CCl_4$ | 0·1 | 17·00 | 2 : 1, 1 : 2 |
| Ar–Cl + Ar–OH | Chlorobenzene | Phenol | $CCl_4$ | 0·1 | 14·85 | 1 : 1 |
| | ,, | | EW ‡ | 0·1 | 20 | 1 : 1 |
| | Hexachlorobenzene | | $CCl_4$ | 0·05 | 12·08 | 1 : 6, 1 : 9 |
| –C(=O)–N< + ArOH | Dimethylformamide | Phenol | $CCl_4$ [25] | 0·1 | 22 | 1 : 1, 1 : 2 |
| | | | B [25] | 0·25 | | 1 : 1 † |
| | | | W [25] | 0·25 | 19·35 | 1 : 1 |
| –N=N– + ArOH | Azobenzene | Benzyl alcohol | $CCl_4$ [25] | 0·1 | 20 | 1 : 1 |
| | | Phenol | B [25] | 0·25 | 19 | 1 : 1, 1 : 2 |
| $–CO_2R$ + Ar–OH | Ethyl acetate | Phenol | $CCl_4$ [25] | 0·1 | 13·11 | 1 : 1 |
| | | 1-Naphthol-5-sulphonic acid | W [25] | 0·04 | 24 | 1 : 1(?) |
| $–CO_2R$ + Ar–Cl | Ethyl acetate | Chlorobenzene | $CCl_4$ ‡ | 0·1 | 14·85 | 1 : 1 |
| | | | EW * | 0·1 | 14 | 1 : 1 |
| | Phenyl acetate | | B ‡ | 0·1 | 21 | 1 : 1 |
| | | | EW ‡ | 0·25 | 14 | 1 : 1 |

* Solvents and references (where no ref. is given, the test is new): B = benzene; D = dioxan; EW = ethanol–water (1 : 1 v/v); T = toluene; W = distilled water. † By dielectric constant measurement. ‡ Giles and Nakhwa, *J. Appl. Chem.*, 1961, **11**, 197.

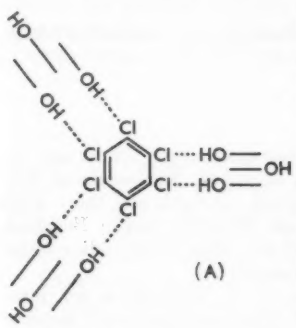
*Experimental.*—The solutes were recrystallised or redistilled, and the solvent was of infrared " AnalaR " quality. A Bellingham and Stanley (Pulfrich) refractometer was used, with water circulation, by suction, from a cool thermostat bath, controlled to $\pm 0{\cdot}01°$ by mercury–toluene regulator. The solutions in each series were aged for several hours in the bath before use, and were selected for test in a random manner, to avoid error due to possible progressive ageing.

The most consistent results are obtained if the refractometer is used by one operator only.

*Comparisons between Results in Carbon Tetrachloride and Bonding Solvents.*—In Table 1 the present results are set alongside others, in which the same type of bond is expected and which were made in bonding solvents. It will be seen that three conditions occur: (*a*) The bonding-ratio of each pair of groups is identical in carbon tetrachloride and in a bonding solvent; this is so for most cases. (*b*) A complex is formed in carbon tetrachloride but not in a bonding solvent; this applies only to aldehyde and ketone groups,

which in water are unreactive, presumably being protected by preferential bonding to the solvent. (*c*) No complex is formed in carbon tetrachloride, though its formation would be expected. This applies to one case only (butyraldehyde–phenol). This was not further investigated, but there are two possible causes: hindrance by the bulky butyl group, or inactivation of the carbonyl-oxygen atom by its intramolecular bonding in a 6-membered ring with hydrogen on the γ-carbon atom. Bonds of the latter type in carboxylic acids and ketones have been suggested by others.[7]

*Complexes with Hexachlorobenzene.*—This compound was used, with phenol, to discover whether high-ratio complexes can be detected in carbon tetrachloride solution. A 1 : 6 complex was expected, in which each chloro-group is bonded to a phenol molecule. In fact, this complex is clearly evident (Fig. 1), but in addition a 1 : 9 complex also appears. We suggest that the latter is formed when three extra phenol molecules each become sandwiched between a pair of those in the 1 : 6 complex (cf. A). There appears to be evidence that this type of structure can be formed between phenol and benzene also, in carbon tetrachloride. These solutes form both 1 : 2 and 2 : 1 complexes: presumably in one case the benzene molecules are sandwiched between two phenol molecules, and in the other phenol is between benzene. These complexes were detected previously,[1] but the test has been repeated for confirmation (Fig. 1).



(A)

*Mixtures not Forming Complexes.*—In the previous papers in this series about twenty systems in carbon tetrachloride were examined, and in nine of these (Table 2) no complex-formation was detected. In most of these nine the pairs of solutes would not be expected to form hydrogen-bond complexes. Systems indicated in Table 2 have now been

TABLE 2.

Systems giving no complex in carbon tetrachloride.

| Solutes | | Total mol. concn. (and ref.) | Temp. |
|---|---|---|---|
| Acetone | Benzoquinone | 0·05 [1] | 20° |
| 2-Acetylpyridine | Di-isobutyl ketone | 0·1 [2b] | 21 |
| Azobenzene | Pyridine | 0·05 [7] | 17 |
| Benzene | Ethylene dichloride | 0·05 [1] | 20 |
| Benzoquinone | Di-isobutyl ketone | 0·05 [1] | 20 |
| Dimethylformamide | Diphenylamine | 0·05 | 13·33 |
| | | 0·05 [2a] | 17 |
| Naphthalene | 2-Naphthol | 0·05 | 13·33 |
| | | 0·1(?) [1] | 20(?) |
| Phenol | Toluene | 0·1 | 17·10 |
| | | 0·1 [1] | 20(?) |
| Pyridine | Triethylamine | 0·1 [1] | 20 |

re-examined at different temperatures, and the previous results confirmed. (A negative result at one temperature only is not conclusive evidence of non-bonding.[1])

## APPENDIX

(By W. GOOD)

*Linearity of Curves.*—In the Appendix of Part II [1] it was demonstrated that curves obtained as here, by the method of " continuous variations," for solutions in which a 1 : 1 complex is formed, should not consist of linear portions, except in the special case where the reaction constant, $K = \infty$. In practice however, all such curves appear to consist of linear portions, even where $K$ must have quite a low value (see, especially, Fig. 1 here). Thus, Flett [8] calculated

[7] *E.g.*, Evans, *J.*, 1936, 785; Evans and Gordon, *J.*, 1938, 1434; Dippy, *J.*, 1938, 1222.
[8] Flett, *J. Soc. Dyers Colourists*, 1952, **68**, 59.

values of $K$ for a wide variety of intermolecular hydrogen-bonding reactions between pairs of organic solutes in carbon tetrachloride at room temperature. These measurements, made from infrared absorption data, on solutions mainly in the range 0·005—1·00M, gave values of $K$ between 3·0 and 150, except for one case (phenol–dimethylformamide) which gave values above 400. The probable explanation for the linearity is as follows.

The curves in Fig. 13 of Part II are calculated from the equation (p. 77 [1]),

$$K = z^r/[(x - pz/r)^p(C - x - qz/r)^q]$$

for the special case where $p = q = r = 1$, *i.e.*, where

$$K = z/(x - z)(c - x - z),$$

and thus they correspond to unit molarity. If the molarity is in fact $1/v$ (*i.e.*, 1 mole in $v$ litres), $z$ should be calculated from the relation

$$K/v = z/(x - z)(c - x - z),$$

*i.e.*, from a curve which in Fig. 13 would be labelled $K/v$.

Thus it is clear that, the more dilute the solutions used, the more nearly linear are the portions of the curve. Conversely, the more concentrated the solutions, the less linear they are; and the limiting case occurs of course when two pure liquids are used, and there is no solvent. This type of system was investigated by, *e.g.*, Pushin and Matavulj, and by Burnham and Madgin, who in fact obtained non-linear curves (hyperbolæ) for values of refractive index against component percentage, by the method of continuous variations.[9]

We thank Professor P. D. Ritchie for his interest, Miss S. P. McGoldrick for some experimental work, the D.S.I.R. for a scholarship (to R. B. McKay), and Imperial Chemical Industries Limited, Central Research Department, and the Commonweal Fund of the Trades House of Glasgow for grants for apparatus.

Department of Chemical Technology, The Royal College of Science and Technology, Glasgow, C.1. [*Received, June 6th*, 1961.]

[9] Pushin and Matavulj, *Z. phys. Chem.*, 1932, *A*, **158**, 290; Burnham and Madgin, *J.*, 1936, 789.

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## 1071. *The Pyrolysis of Decaborane.*

By A. J. Owen

The kinetics of the pyrolysis of decaborane have been investigated for a static system in the temperature range 210—250° and at decaborane pressures 60—600 mm. Hg. The decomposition leads to non-volatile solid hydrides and hydrogen; its rate is of the first order with respect to decaborane, slightly retarded by hydrogen; the activation energy is 41·6 ± 0·5 kcal./mole. Hydrogen is also formed by decomposition of the non-volatile solid hydrides, and its rate of formation in this way is strongly retarded by hydrogen. A mechanism for the formation of non-volatile solid hydrides is proposed and discussed.

The pyrolysis of decaborane to non-volatile solid hydrides and hydrogen was investigated as part of the general study of the synthesis of the higher boron hydrides from diborane. In previous work [1] it was suggested that the non-volatile solid hydrides produced during pyrolysis of diborane originated from decaborane. While it is known that they are formed at low temperatures (~100°) by the reaction of diborane with pentaborane [2] or decaborane [3] no information on the mechanism or reaction rates at the temperature (~240°) of pentaborane synthesis is available. The present work was therefore undertaken to supplement the knowledge of their formation.

[1] Owen, *J. Appl. Chem.*, 1960, **10**, 483.
[2] Hillman, Mangold, and Norman, Abs. 133rd Meeting Amer. Chem. Soc., San Francisco, 1958, p. 18.
[3] Shapiro and Williams, *J. Amer. Chem. Soc.*, 1959, **81**, 4787.

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The pyrolysis of decaborane was first described by Stock and Pohland [4] who found that it did not decompose appreciably at 200°, but did so extensively at 250°, to give non-volatile solids of approximate composition $(BH_{0\cdot6})_x$. Beachell and Haugh [5] made a kinetic investigation of the system over the temperature range 170—238°, on the basis almost entirely of pressure measurements, from which they concluded that, in the initial stages, the reaction was of the first order with respect to diborane and was retarded by hydrogen. No detailed mechanism was proposed. Siegal and Mack [6] also studied the pyrolysis of decaborane; although their work was not intended to be of a kinetic nature, a plot of their results of time against percentage decomposition at 200° with an initial decaborane pressure of ~240 mm. gave a straight line, suggesting that the reaction was of zero order; but this will be shown to be due to their method of calculating the percentage decomposition from the hydrogen evolved.

## Experimental

Pure decaborane, m. p. 99·7°, was obtained from an impure sample (American Potash and Chemical Co.) by crystallisation from hexane followed by vacuum-sublimation. By oxidation with potassium persulphate in alkaline solution and titration of the boric acid formed,[7] it was shown to have a purity of at least 99·5%. Hydrogen and "White Spot" nitrogen were obtained from cylinders and were dried.

Experiments were carried out in Pyrex reaction vessels having a total volume of ~150 c.c. They consisted of a reaction bulb, a freezing nipple, and an entry tube, 15 cm. long, comprising a B10 cone on the end of a 7 cm. stem of a B14 cone. Decaborane was introduced into the weighed reaction vessel of known volume by means of a funnel which prevented it from adhering to the side of the inlet tube. After weighing, the tubing between the glass joints was drawn down to a coarse capillary, and the reaction vessel connected to the vacuum line by the B10 joint, evacuated, and sealed at the top of the constriction. In the experiments on retardation by hydrogen and on alkylation, a known pressure of hydrogen or alkylating agent was admitted before the sealing. No detectable amount of decaborane was lost during this process.

The filled reaction vessels were placed in a well-stirred "Aroclor" bath, the surface of which was covered with pear-shaped glass globes to minimize the escape of the vapour. Electric fire-bars inserted in metal tubes in the bottom of the bath supplied heat to the bath. The temperature of the bath was controlled within $\pm 0\cdot5°$ by means of a bimetal switch in conjunction with an on-off Sunvic control operating on one of the fire-bars. Experiments were carried out for varying times at 210°, 230°, and 250° and initial decaborane pressures of 60, 120, 300, and 600 mm. Similar pressures of hydrogen were added in the retardation experiments. At the end of an experiment the reaction vessels were removed from the bath and rapidly cooled to room temperature, then connected, by means of the B14 ground-glass joint, to a seal-breaker on the vacuum line, and then opened.

Hydrogen was analysed by pressure-measurement after expansion of the gas into a known volume. The reaction vessel was then filled with dry nitrogen and removed from the vacuum line. Two methods, both giving identical results, were used to analyse the residue. Unchanged decaborane was (*a*) extracted from the solid products with dry benzene, or (*b*) sublimed from the evacuated vessel at 100°; in both cases the decaborane was subsequently estimated by the quinoline colorimetric method.[8] The reaction vessel containing the solid hydrides which remained after sublimation of the decaborane was connected by means of the B14 ground-glass joint to a mercury manometer of known volume and after evacuation heated to the reaction temperature; the rate of evolution of hydrogen was measured. Similar experiments were made with an initial hydrogen pressure equivalent to that developed in the main reaction of decaborane. Finally, the boron content non-volatile of the solid hydrides was determined by oxidation with alkaline persulphate.[7]

[4] Stock and Pohland, *Ber.*, 1929, **62**, 90.
[5] Beachell and Haugh, *J. Amer. Chem. Soc.*, 1958, **80**, 2939.
[6] Siegal and Mack, *J. Phys. Chem.*, 1958, **62**, 373.
[7] Dunstan and Griffiths, M.O.A. unpublished report.
[8] Hill and Johnston, *Analyt. Chem.*, 1955, **27**, 1300.

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## Results

The results are given in Figures 1—3.

*Order of Reaction.*—The course of the reaction is illustrated in Fig. 1 by a typical set of results obtained at 230° and an initial decaborane pressure of 300 mm. The decomposition of decaborane and the formation of hydrogen are shown by the lower and the upper continuous curve, respectively. The rate of decomposition of decaborane falls off gradually with time and the reaction is shown to be of the first order by first-order graphs (Fig. 2) drawn at 210°, 230°, and 250° over a range of initial decaborane pressures from 60 to 600 mm. Straight lines can only be drawn through points up to 60% reaction (corresponding to log $[a/(a - x)] = 0{\cdot}4$). Above this conversion the reaction tends to be of greater than first order.

Decomposition of the non-volatile solid hydrides formed from decaborane also occurs and gives a polymeric material and hydrogen. This accounts for the fact that the rate of formation of hydrogen is much greater than that of decomposition of decaborane, especially in the later stages of the reaction, as illustrated in Fig. 1. It is probable that the non-volatile solid

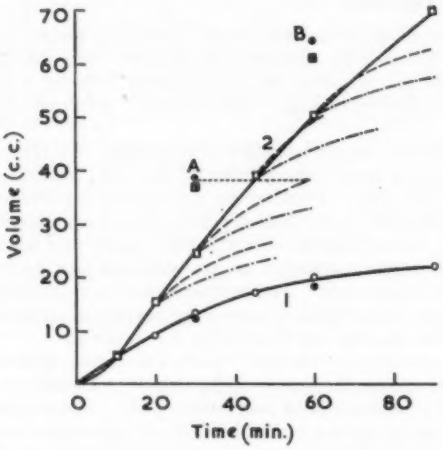



FIG. 1. Course of the decomposition of decaborane.

Temp. 230° C; $p^\circ_{B_{10}H_{14}} = 300$ mm.

1, Decaborane reacted.
2, Hydrogen formed.

—— Hydrogen formed from non-volatile solid hydride at $p^\circ_{H_2} = 0$.
—·— Hydrogen formed therefrom at $p^\circ_{H_2} = p_{H_2}$ in reaction.

hydrides decompose according to a first-order law, since the hydrogen evolved at a given time is directly proportional to the initial pressure of decaborane.

*Retardation by Hydrogen.*—Examples of the retarding effect of hydrogen on (*a*) the rate of decomposition of decaborane and (*b*) the rate of formation of hydrogen are given in Fig. 3, where the volume of gas that reacted or was formed is plotted against the average pressure of hydrogen at 230°, with an initial decaborane pressure 300 mm. and reaction times of 10 and 30 min. After 10 min. the small retardation effect is almost identical for both the rate of decomposition of decaborane and the rate of formation of hydrogen. This would be expected if one molecule of decaborane decomposed to give one molecule of hydrogen, because in the early stages of the reaction the concentration of non-volatile solid hydrides is low and the rate of formation of hydrogen from them is small. In the later stages of the reaction, *i.e.*, after 30 min., the retardation is much more pronounced for hydrogen than for decaborane, owing to marked inhibition by hydrogen of the decomposition of the non-volatile solid hydrides.

*The Activation Energy.*—An Arrhenius plot leads to an activation energy of $41{\cdot}6 \pm 0{\cdot}5$ kcal./mole, in excellent agreement with the value of 41·4 kcal./mole obtained by Beachell and Haugh.[5]

*Stoicheiometry of the Initial Steps.*—It has already been pointed out that after a short initial reaction period hydrogen is produced much more rapidly than decaborane decomposes. Attempts were made to examine the rate of formation of hydrogen in the decomposition of the non-volatile solid hydrides alone, using hydrides which remained after the decaborane had been sublimed. The reaction vessel was connected to a manometer, evacuated, and heated at the reaction temperature for 30 min., the rate of gas evolution being followed on the

manometer. The results are shown in Fig. 1 by the broken lines (---). They show that in the later stages of the decomposition of decaborane, *i.e.*, where there is a relatively large quantity of hydrides produced, the rate of formation of hydrogen in the complex overall reaction appears to be less than the rate of formation of hydrogen from the hydrides produced alone. The experiments were then repeated but extra hydrogen was added to the non-volatile solid hydrides so that the hydrogen pressure was that obtaining at the given time during the order experiments. The results of these experiments, shown as dot-dash curves (·—·—), indicate the marked inhibiting effect of hydrogen in the decomposition of the non-volatile solid hydrides. Comparison of the rates of formation of hydrogen from the non-volatile solid hydrides and that from the total reaction with the rate of decomposition of decaborane at 210°, 230°, and 250°

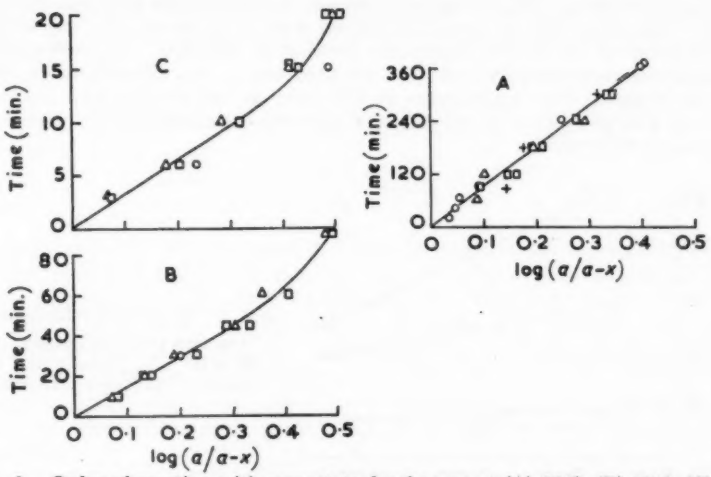



FIG. 2. Order of reaction with respect to decaborane at (A) 210°, (B) 230°, (C) 250°. ○, $p°_{B_{10}H_{14}} = 600$ mm. □, $p°_{B_{10}H_{14}} = 300$ mm. △, $p°_{B_{10}H_{14}} = 120$ mm. +, $p°_{B_{10}H_{14}} = 60$ mm.

(initial decaborane pressure 300 mm. and various reaction times) is given in the Table. The difference between the rate of formation of total hydrogen and the rate of decomposition of decaborane, $d(H_2, \text{total})/dt + d(B_{10}H_{14})/dt$, is given almost exactly by the rate of evolution

Rate of formation of hydrogen from decaborane and non-volatile solid hydrides: initial pressure of decaborane = 300 mm.

| Temp. | Time (min.) | $\frac{d(H_2)\text{ total}}{dt}$ (c.c./min.) | $\frac{-d(B_{10}H_{14})}{dt}$ (c.c./min.) | $\frac{d(H_2)\text{ total}}{dt} + \frac{d(B_{10}H_{14})}{dt}$ (c.c./min.) | $\frac{d(H_2)\text{N.V.S.H.}}{dt}$ No initial $H_2$ (c.c./min.) | $\frac{d(H_2)\text{N.V.S.H.}}{dt}$ Added $H_2$ (c.c./min.) |
|---|---|---|---|---|---|---|
| 210° | 120 | 0·138 | 0·083 | 0·055 | 0·083 | 0·060 |
| | 180 | 0·134 | 0·057 | 0·077 | 0·107 | 0·074 |
| | 240 | 0·117 | 0·042 | 0·075 | 0·107 | 0·074 |
| | 300 | 0·100 | 0·032 | 0·068 | 0·123 | 0·062 |
| 230 | 20 | 1·02 | 0·460 | 0·560 | 0·600 | 0·500 |
| | 30 | 0·950 | 0·375 | 0·575 | 0·620 | 0·500 |
| | 45 | 0·850 | 0·200 | 0·650 | 0·817 | 0·620 |
| | 60 | 0·650 | 0·110 | 0·540 | 0·666 | 0·507 |
| 250 | 3 | 5·15 | 2·32 | 2·83 | 2·3 | 2·2 |
| | 6 | 4·95 | 1·68 | 3·27 | 3·4 | 3·2 |
| | 10 | 3·55 | 0·83 | 2·72 | — | 2·6 |
| | 15 | 2·28 | 0·43 | 1·85 | 2·2 | 1·7 |
| | 20 | 1·85 | 0·29 | 1·56 | 2·0 | 1·4 |

of hydrogen from the non-volatile solid hydrides in the presence of the initially added pressure of hydrogen. It is significant that the rate of evolution of hydrogen from the non-volatile solid hydrides in the absence of initially added hydrogen approaches the other rates at low reaction times, *i.e.*, when there is only a relatively small quantity of hydride products and the initial hydrogen pressure is low. The initial step in the thermal decomposition of decaborane, therefore, requires that one molecule of hydrogen is formed for every molecule of decaborane decomposed: $xB_{10}H_{14} = (B_{10}H_{12})_x + xH_2$.

In order to gain a clearer picture of the reaction mechanism, decaborane and the non-volatile solid hydrides were heated together. The reaction vessels were modified in these experiments so that the entry tube was a double set of ground-glass joints, the outer set of joints being utilised in obtaining a sample of non-volatile solid hydride as a surface coating inside the reaction vessel. This sample was prepared by heating 300 mm. decaborane at 230° for 30 min. The second set of joints was utilised when more decaborane was weighed into the reaction vessel to return the decaborane pressure to 300 mm. The non-volatile solid hydrides were thus never handled and were subjected only to dry nitrogen during the weighing. The durations of these experiments at 230° were 30 and 60 min. and the results are plotted in Fig. 1 by the points ⊕ and ⊞ which represent the decaborane decomposed and the hydrogen formed, respectively.

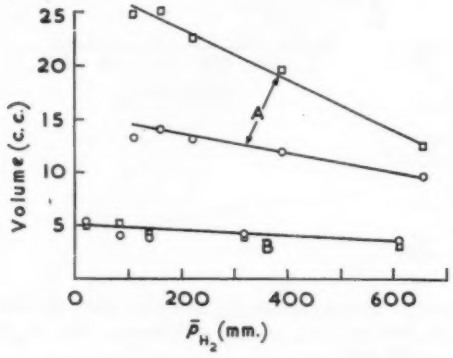



FIG. 3. Hydrogen retardation. 1, Reaction time (A) 30 min, (B) 10 min. ○, Decaborane reacted; □ hydrogen formation.

The amount of decaborane decomposed is very close to that decomposed in the absence of non-volatile solid hydrides, the slightly lower values being consistent with a small retardation due to the increased hydrogen pressure developed by the hydrides produced. Although the hydrogen evolved is much less than the theoretical points A and B (obtained by addition of the hydrogen evolved from the initial non-volatile solid hydrides to the hydrogen normally produced in the decomposition experiments for reaction times of 30 and 60 min., respectively), the result is consistent with the retarding effect of hydrogen on the hydrogen evolution from the non-volatile solid hydrides. These two experiments show that the reaction of decaborane with the solid hydrides produced from it is so slow that it need not be considered in the proposed reaction mechanism.

## DISCUSSION

*Reaction Mechanism.*—The following mechanism is proposed to explain the experimental facts.

$$B_{10}H_{14} + B_{10}H_{14} \underset{k_2}{\overset{k_1}{\rightleftharpoons}} B_{10}H_{14}^* + B_{10}H_{14} \quad . \quad . \quad . \quad . \quad . \quad (1)$$

$$B_{10}H_{14}^* \underset{k_4}{\overset{k_3}{\rightleftharpoons}} B_{10}H_{12} + H_2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

$$B_{10}H_{14} + B_{10}H_{12} \underset{k_6}{\overset{k_5}{\rightleftharpoons}} B_{20}H_{24} + H_2 \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

$$B_{20}H_{24}(g) \rightleftharpoons B_{20}H_{24}(s) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

$$2B_{20}H_{24} \rightleftharpoons H_2 + \text{Non-volatile solid hydrides} \quad . \quad . \quad . \quad . \quad (5)$$

In the steady state, assuming $k_3 \ll k_2[B_{10}H_{14}]$, we have

$$-\frac{d[B_{10}H_{14}]}{dt} = k_5[B_{10}H_{14}][B_{10}H_{12}] - [H_2](k_4[B_{10}H_{12}] + k_6[B_{20}H_{24}]) \quad . \quad (6)$$

Since it has been shown experimentally that hydrogen has only a small effect on the rate of reaction of decaborane, the hydrogen retardation term can be neglected. If the rate of reaction of the intermediate $B_{10}H_{12}$ with decaborane is faster than the other reactions, the rate-determining step will be the formation of the intermediate which is given by the expression

$$\frac{d[B_{10}H_{12}]}{dt} \text{ formation} = \frac{k_1k_3}{k_2}[B_{10}H_{14}] + \frac{k_3k_4}{k_2} \cdot \frac{[B_{10}H_{12}][H_2]}{[B_{10}H_{14}]}$$

$$\simeq \frac{k_1k_3}{k_2}[B_{10}H_{14}]$$

Under these conditions the reaction is of first order with respect to decaborane.

As the reaction proceeds the concentration of decaborane decreases, and it can be shown that for suitable values of $k_5$ and $k_1k_3/k_2$, the rate of formation of the intermediate $B_{10}H_{12}$ will become closer to the rate of its subsequent reaction with decaborane. Eventually the term $k_1k_3[B_{10}H_{14}]/k_2$ will be greater than $k_5[B_{10}H_{14}][B_{10}H_{12}]$ and will result in deviations from the first-order expression. These deviations should be greatest in the experiments carried out at the lower initial decaborane pressures. Unfortunately, the experimental error is too large for the effect of variation of initial decaborane pressures to be seen in Fig. 2.

The decomposition of the non-volatile solid hydrides represented by equation (5) is very complex, and no detailed examination of this reaction was made in the present work. However, the retardation of the hydrogen evolution from those hydrides by hydrogen, originally observed by Shapiro and Williams,[3] is interesting. Since the effect is restricted to hydrogen,[5] the reaction must be to some extent reversible. It is conceivable that the polymer, on heating, loses hydrogen and becomes a free radical. Subsequently the radicals could either recombine with the hydrogen, or irreversibly dimerise. This speculative reaction would account for the observed kinetic phenomenon.

The results quoted in this paper are in qualitative agreement with those of other workers.[5,6] Quantitatively, however, the hydrogen-retardation effect on the rate of decomposition of decaborane is much smaller than that reported by Beachell and Haugh.[5] For example, in their work, the rate constant at 220° and a decaborane pressure of 268 mm. decreased linearly from $9{\cdot}8 \times 10^{-3}$ min.$^{-1}$ at zero initial hydrogen pressure to $3{\cdot}0 \times 10^{-3}$ min.$^{-1}$ at 600 mm. initial hydrogen pressure. The nearest corresponding conditions in the present work were at 230° and a decaborane pressure of 300 mm., when the rate constant decreased from $1{\cdot}60 \times 10^{-2}$ to $1{\cdot}16 \times 10^{-2}$ min.$^{-1}$ for the corresponding hydrogen pressures. Obviously the discrepancy has arisen through the different methods of analysis employed in the two studies. In fact, Beachell and Haugh have stated that their rate constants were calculated from the pressure measurements of "all boron hydridic materials ($P_{BH}$)." It is possible that the intermediate $B_{20}H_{24}$ proposed for the present reaction mechanism would appear in greater concentration when the pressure of initial hydrogen is increased and thus magnify the true retardation effect on the rate of decomposition of decaborane.

Siegal and Mack's results[6] are misleading because the values they give for the

percentage decomposition of decaborane are based on the amount of hydrogen evolved and the wrong assumption that a constant 2 molecules of hydrogen are evolved for each molecule of decaborane decomposed. Thus, a plot of the percentage decaborane decomposed against time would lead to a graph very similar in shape to that given by the hydrogen curve in Fig. 1, and not inconsistent with the zero-order kinetics mentioned previously.

The proposed mechanism accounts for all the available experimental results. Beachell and Haugh [5] have shown that hydrogen radicals do not participate in the reaction and it has therefore been assumed that the first step leads to the splitting off of a hydrogen molecule. Using the infrared absorption bands for various pyrolysis products they showed also that the initial hydrogen break did not involve a bridge hydrogen atom, but they were uncertain of the site at which the break occurred. However, comparison of the reaction of decaborane and ethyl bromide with the pyrolysis of decaborane under similar conditions (230° with a reaction time 5 min. and decaborane pressure 300 mm.) gave an almost identical conversion of decaborane (8%). In the alkylation experiment the product consisted of 2-ethyldecaborane and a trace of non-volatile solid hydrides, which suggests that the initial step in the decomposition of decaborane involves the breaking of the 2-BH bond. Further work on the kinetics of the alkylation of decaborane is in hand to test this view.

Additional evidence indicating that the initial break involves the 2-position has been obtained during an attempt to isolate the intermediate product $B_{20}H_{24}$. Vacuum sublimation at 100° of the solid products prepared at 230° enables all the unchanged decaborane to be removed, and subsequent vacuum distillation at 210° afforded a very small quantity of a viscous liquid. This liquid has an infrared spectrum very similar to that of decaborane but has such a low volatility that it was not recovered from a 3-ft. gas-chromatographic column [9] even after 7 hours. It is therefore believed to be the $B_{20}H_{24}$ intermediate. For material of this high molecular weight to exist as a liquid at room temperature, its structure would be expected to be highly unsymmetrical, possibly joined between the 2- and the 6-positions; it should not be the eicosahedron previously suggested to account for the impurity lines in the mass spectrum of decaborane.[10]

One of the objects of this work was to see if the decomposition of decaborane made any significant contribution towards the formation of non-volatile solid hydrides on pyrolysis of diborane at ~240°. It can be shown that at 240°, with 1 : 5 diborane : hydrogen, total flow rate 400 c.c./min., in a 12-unit multistage pyrolyser,[1] only about 0·1% of decaborane is converted by thermal decomposition alone into non-volatile solid hydrides. This is considerably less than is observed in practice,[1] and it is probable that the solid non-volatile hydrides formed during the pyrolysis of diborane originate in a reaction of diborane with decaborane.[3]

The author thanks Mr. R. J. Pace for carrying out the infrared and decaborane analysis.

MINISTRY OF AVIATION, EXPLOSIVES RESEARCH AND DEVELOPMENT ESTABLISHMENT,
WALTHAM ABBEY, ESSEX. [*Received, June 12th*, 1961.]

[9] Blay, Williams, and Williams, *J.*, 1960, **81**, 424.
[10] Quayle, *J. Appl. Chem.*, 1959, **9**, 395.

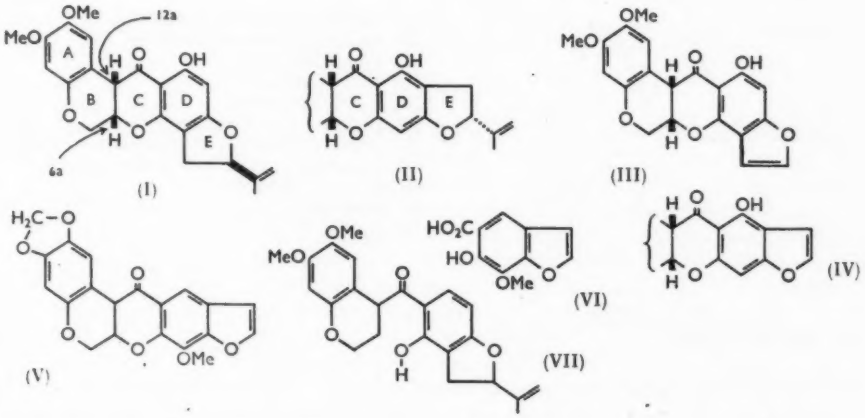
## 1072. *Structure and Stereochemistry of Sumatrol and Malaccol.*

By L. Crombie and R. Peace.

The angular orientation of the D/E rings of natural malaccol and natural sumatrol is established. (±)-Malaccol, however, is of the linear D/E form, and the two reported 6a,12a-dehydromalaccols, both of m. p. 257°, are linear and angularly fused forms. Optical rotatory dispersion correlations with natural rotenone indicate the stereochemistry shown in (I) for sumatrol and in (III) for malaccol.

Degradative study of the natural rotenoids, (−)-sumatrol [1,2] and (+)-malaccol [3,4] [sign of rotation refers to benzene solution], has led to the alternatives (I) or (II) for the former and (III) or (IV) for the latter [without the stereochemical designation]. The angularly fused forms (I) and (III) were preferred by earlier workers mainly because of analogy with the very limited number of known natural rotenoids. Later discovery of pachyrrhizone [5] (V), with a linear D/E system, weakened the inference and makes experimental decision desirable.

The linear or angular fusion of 11-unsubstituted rotenoids is easily decided as the 10,11-hydrogen atoms are spin coupled and give rise to a quartet in the nuclear magnetic



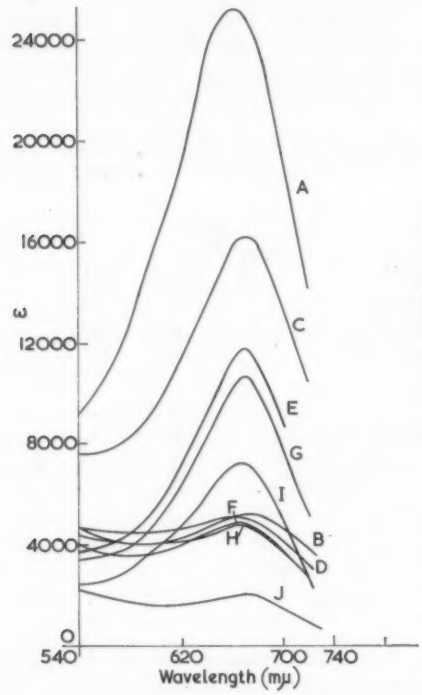

resonance spectra of angular forms.[6] This test is not available for the 11-hydroxyrotenoids, but indophenol formation [7] (Gibbs reaction) provides suitable evidence. As a qualitative test for the presence of a free position *para* to an aromatic hydroxyl group, the reaction can be capricious and we have employed spectrophotometric control.[8] The data have been used more restrictively than usual in that (*a*) the validity of the method was first tested on a pair of established linear and angularly fused D/E 11-hydroxyrotenoids, and (*b*) decision on the two unknown rotenoids is reached by comparison of their linear and angularly fused forms.

The angular D/E fusion of natural (−)- and (±)-α-toxicarol (VIII) and the linear

[1] Robertson and Rusby, *J.*, 1937, 497.
[2] Kenny, Robertson, and George, *J.*, 1939, 1601.
[3] Harper, *J.*, 1940, 309.
[4] Harper, *J.*, 1942, 593.
[5] Bickel and Schmid, *Helv. Chim. Acta*, 1953, **36**, 664.
[6] Crombie and Lown, unpublished work.
[7] Gibbs, *J. Biol. Chem.*, 1927, **72**, 649.
[8] King, King, and Manning, *J.*, 1957, 563.

fusion of (±)-β-toxicarol (IX) are rigorously established [9,10] and as expected the infrared spectra of solutions of the first two are identical and differ considerably from that of the last. The figure shows the spectra of the Gibbs reaction products from (±)-β-toxicarol (curve E) with a free position *para* to the hydroxyl group, and from (−)- or (±)-α-toxicarol with a blocked *para*-position (curve F).* Clear differentiation between the two types of fusion is obviously possible.

Natural (+)-malaccol, when boiled with ethanolic sodium acetate, is racemised, and the (±)-product, m. p. 244°, has been accepted as having an unaltered skeleton.[3] We find, however, that the infrared spectrum of its solution differs from that of the (−)-form, and one compound must have the linear and the other the angular fusion, the D/E arrangement being altered because of the two possible ways of re-closing the ion from (X) which results




(A) 6a,12a-Dehydro-β-malaccol.
(B) 6a,12a-Dehydro-α-malaccol.
(C) (±)-β-Malaccol.
(D) (+)-α-Malaccol.
(E) (±)-β-Toxicarol.
(F) (−) or (±)-α-Toxicarol.
(G) Natural sumatrol after treatment with sodium acetate (see Experimental).
(H) (−)-α-Sumatrol.
(I) Rotenol.
(J) " Acid P."

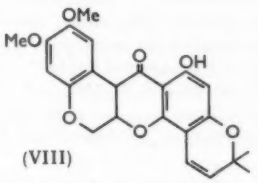
from treatment with base. Natural (+)-malaccol (α-malaccol) is the angular form (III) (curve D) whereas (±)-malaccol, m. p. 244° [now referred to as (±)-β-malaccol], is the linear form (IV) (curve C). This result throws new light on the 6a,12a-dehydromalaccols, the status of which has been obscure.[3] If natural (+)-malaccol is first refluxed with alcoholic sodium acetate and is then treated with iodine and finally zinc, a dehydromalaccol, m. p. 257°, is obtained; (±)-β-malaccol gives a similar product. If, however,

* The structure of pachyrrhizone and its degradation product " acid P " (VI) seem securely founded.[5] The " acid P," however, is reported to give a positive blue-violet Gibbs reaction [5] which would support an alternative structure. When examined by the technique used here " acid P " gave curve J, consistent with formulation (VI). For comparison, rotenol (VII),[11] with a free *para*-position, gave curve I. The specimen of " acid P " was provided by Professor H. Schmid, to whom we express our thanks.

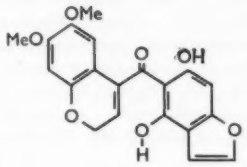
[9] George and Robertson, *J.*, 1937, 1535.
[10] Cahn, Phipers, and Boam, *J.*, 1938, 513.
[11] Crombie, Godin, Whiting, and Siddalingaiah, *J.*, 1961, 2876.

(+)-malaccol is treated with sodium acetate and the iodine is added rapidly, a dehydromalaccol also having m. p. 257°, but giving a large m. p. depression with the former, is isolated.[3] The infrared spectra of their solutions are different. Curve A shows that the first method gives, as expected, a linearly D/E-fused 6a,12a-dehydro-compound (cf. IV) whilst the second procedure gives the corresponding angular α-form (cf. III) (curve B).

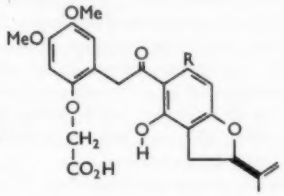
Curve H shows that natural (−)-sumatrol belongs to the angularly fused D/E class (I). Treatment of this with mild base can theoretically give a mixture of four linear and four angular D/E stereoisomers, but if compounds having the thermodynamically unstable B/C fusion are discounted, this is reduced to four. Curve G shows the spectrum of the indophenols derived from the product isolated from such treatment with base. The product is largely, if not entirely, linearly D/E-fused, though separation of the individual diastereoisomers has not been undertaken because of the small supply of (−)-sumatrol available.



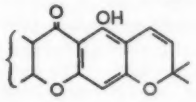

(VIII)




(X)

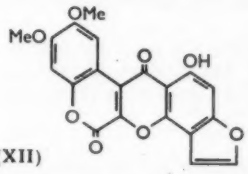



(XI)




(IX)

Professor W. Klyne has kindly compared the optical rotatory dispersion of sumatrolic acid [1] (XI; R = OH) with derrisic acid (XI; R = H) derived from natural rotenone. Both have the same type of negative plain curve, indicating that the 5′ centre of sumatrol has the same absolute configuration as in rotenone. This result has recently been confirmed by Professor C. Djerassi and Dr. W. D. Ollis who have also shown that 11-acetylsumatrol [12] and sumatrol [13] have a positive Cotton effect superimposed on the above negative plain curve. Rotenone also shows a positive Cotton effect [12] so that the stereochemistry of sumatrol appears to be the same as that of rotenone,[14] *i.e.*, 6aβ, 12aβ,5′β (I). Malaccol has recently been examined for us by Professor Djerassi and also has a positive Cotton effect: it too must therefore be 6aβ, 12aβ (III).




(XII)

## Experimental

*Materials Used.*—Natural malaccol had m. p. 244—246°, $[\alpha]_D^{20}$ +190° (*c* 1·2 in chloroform) {lit.,[3] m. p. 225°, remelting as (±)-malaccol (racemisation) at 244°, $[\alpha]_D^{18}$ +190° (1·02 in chloroform)}. Natural sumatrol had m. p. 196—198° $[\alpha]_D^{20}$ −182° (*c* 2·84 in benzene) when freshly recrystallised: the m. p. was unaltered after storage for some days; {lit.,[1] m. p. 192—194°, 195—196° after storage for 3 days: $[\alpha]_D$ −184° (*c* 1·335 in benzene)}. Natural toxicarol had m. p. 104° (from ethyl acetate–ethanol), $[\alpha]_D^{19}$ −67·5° (*c* 2·25 in benzene) {lit.,[13] m. p. 103°, $[\alpha]_D^{20}$ −67° (benzene)}. (±)-α-Toxicarol had m. p. 218—219°, and (±)-β-toxicarol m. p. 166—167° [lit.,[10] m. p. 219° and 165—167°, respectively].

*Procedure for Gibbs's Reaction.*—The weighed sample (approx. 2 mg.) in "AnalaR" pyridine (1 ml.) was treated with a fresh solution of 2,6,*N*-trichloro-*p*-benzoquinoneimine in pyridine (5 ml. of 0·2% solution) and diluted to 125 ml. with sodium borate buffer (pH 9·2). Spectral

[12] Djerassi, Ollis, and Russell, *J.*, 1961, 1448.
[13] Djerassi and Ollis, personal communication.
[14] Büchi, Crombie, Godin, Kaltenbronn, Siddalingaiah, and Whiting, *J.*, 1961, 2843.

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curves were measured by a Unicam S.P. 600 instrument against a cell containing the reagent system without the sample. The curves shown in the Figure were all measured at 20 min. as $\varepsilon_{max.}$ values change with time. This was investigated for most of the samples and is illustrated as follows:

| | 20 min. | 40 min. | 60 min. | 80 min. |
|---|---|---|---|---|
| α-Toxicarol | 4900 | 5200 | 5400 | — |
| β-Toxicarol | 11,900 | 12,500 | 12,600 | 12,800 |

There was little change in $\lambda_{max.}$, 670—675 mμ.

Besides the compounds in the Table, compounds of the rotenonone type derived from malaccol [m. p. 301° (decomp.)] (*i.e.*, XII) and α-toxicarol [m. p. 284—285° (decomp.)] were examined. These gave no maximum in the Gibbs reaction curve, but the rotenonone type of compound from β-toxicarol had $\lambda_{max.}$ 710 mμ. The compounds were made by oxidation of the parent rotenoids by active manganese dioxide [11] and we thank Dr. P. J. Godin for these measurements.

(±)-β-*Malaccol.*—(+)-α-Malaccol (50 mg.) was refluxed in acetone (2 ml.), containing potassium carbonate (100 mg.), for 2 hr. The mixture was poured into water, and just acidified, and the product was crystallised from chloroform–ethanol to give pale yellow needles, m. p. and mixed m. p. with an authentic specimen of " (±)-malaccol " 249°.[3] (±)-β-Malaccol had $\lambda_{max.}$ (in ethanol) 248i, 253, 288, and 357 mμ (ε 30,300, 36,100, 15,100, and 1800), $\nu_{max.}$ (in chloroform) 1653, 1629, and 1590 cm.$^{-1}$. (+)-α-Malaccol had $\lambda_{max.}$ (in ethanol) 246, 253·5, 264i, 287, and 362 mμ (ε 29,200, 34,100, 13,600, 12,000, and 2500), $\nu_{max.}$ (chloroform) 1645, 1623i, and 1605 cm.$^{-1}$.

6*a*,12*a*-*Dehydro*-α-*malaccol.*—Natural α-malaccol (100 mg.), suspended in boiling alcohol (10 ml.) containing iodine (200 mg.), was refluxed for 1 hr. with sodium acetate (200 mg.) in ethanol (4 ml.). The yellow product (105 mg.) was refluxed with zinc dust (100 mg.) in acetic acid (2 ml.) for 2 hr., more zinc (50 mg.) being added during the reaction. The mixture was filtered and, on cooling, deposited 6a,12a-dehydro-α-malaccol, m. p. 246—250° (from chloroform–ethanol), m. p. 258° (after sublimation), $\lambda_{max.}$ (in ethanol) 233, 240i, 257, and 315 mμ (ε 28,300, 27,900, 27,000, and 14,700), $\nu_{max.}$ (in chloroform) 1656, 1613, and 1592 cm.$^{-1}$. Harper gives m. p. 257°.[3] The compound depressed to 236° the m. p. of 6a,12a-dehydro-β-malaccol [3] (m. p. 257°), $\lambda_{max.}$ (in ethanol) 235i, 260, 275, and 312 mμ (ε 22,000, 32,000, 32,000, and 16,800), $\nu_{max.}$ (in chloroform) 1658, 1626, and 1600 cm.$^{-1}$.

*Treatment of* (−)-*Sumatrol with Sodium Acetate.*—Natural sumatrol (50 mg.) was refluxed with ethanol (10 ml.) containing sodium acetate (100 mg.) for 2 hr. The product (50 mg.) had m. p. 160—170° and crystallised from chloroform–ethanol (1 : 3) to give a stereoisomeric mixture (15 mg.), m. p. 183—190°, which was used to obtain curve (G).

We are grateful to Professor S. H. Harper for gifts of natural malaccol and its derivatives, and to Professor W. Klyne, Professor C. Djerassi, and Dr. W. D. Ollis for optical rotatory dispersion information. One of us (R. P.) is grateful to the Department of Scientific and Industrial Research for a postgraduate award.

Department of Chemistry, University of London, King's College,
Strand, W.C.2. [*Received, June 22nd,* 1961.]

## 1073. *The Gaseous Reaction of Chlorine Trifluoride with Methane.*

By C. F. Cullis and C. B. Baddiel.

Minimum ignition temperatures, measured at pressures from 80 to 600 mm., show that a 3 : 2 mixture of methane and chlorine trifluoride is the most prone to explosion. A characteristic property, which persists even in packed vessels or in the presence of an excess of inert diluent, is the very sudden transition from negligibly slow to explosively rapid reaction. The kinetic features of the slow reaction cannot therefore be determined and analytical studies are confined to the products of the explosive reaction.

Under all conditions, hydrogen fluoride is much the most abundant gaseous product and methyl chloride is the predominant organic product. After explosion of pure reactant mixtures, considerable amounts of acetylene, ethylene, and ethane are formed, together with smaller quantities of some fully halogenated methanes. In the presence of an excess of nitrogen, the production of $C_2$ hydrocarbons is largely suppressed and certain partly halogenated methanes become important organic products.

It is concluded that the reaction occurs by a free-radical chain mechanism. The analytical results suggest that the chlorine trifluoride acts primarily by " stripping off " of hydrogen from the hydrocarbon by the combined fluorine. The probable mode of formation of the principal organic products is also discussed.

For some time after the discovery of the halogen fluorides,[1] their reactions with organic compounds were little studied. In earlier attempts to use these compounds as halogenating agents, attention was paid chiefly to bromine trifluoride [2,3] and iodine pentafluoride,[3,4] but in recent years, there have been several investigations concerned with the use of the more highly reactive chlorine trifluoride for this pupose.[5] In many cases, the principal object of such work has been the preparation of polyhalogen (and, if possible, perhalogen) compounds for use as chemically inert lubricants, and most of these studies have yielded little fundamental information regarding the reactions taking place. Musgrave and his co-workers, in an attempt to obtain some insight into the mechanism of halogenation by chlorine trifluoride, made more detailed investigations of its reaction with benzene and some of its derivatives [6] and with trichloroacetic acid and the corresponding acid chloride.[7]

These researches and indeed almost all previous work on the reactions of chlorine trifluoride with organic compounds have been carried out in the liquid phase, the halogen fluoride, often diluted with nitrogen, being bubbled into the liquid organic compound or its solution in a suitable solvent. Apart from some unpublished work,[8] on the halogenation of benzene in the vapour phase, which evidently exhibits some marked differences from the corresponding liquid-phase reaction, little or no information appears to be available regarding the gaseous interaction of chlorine trifluoride with organic compounds. For several years, some work has been in progress in these laboratories on the reactions of this interhalogen compound with gaseous paraffin hydrocarbons and the present paper describes some results obtained with the chlorine trifluoride–methane system.

[1] Ruff *et al.*, *Z. angew. Chem.*, 1928, **41**, 1289 *et seq.*; *Z. anorg. Chem.*, 1928, **176**, 258 *et seq.*
[2] Nutting and Petrie, U.S.P. 1,961,622; McBee, Lindgren, and Ligett, *Ind. Eng. Chem.*, 1947, **39**, 378; U.S.P. 2,432,977, 2,471,831.
[3] Banks, Emeléus, Haszeldine, and Kerrigan, *J.*, 1948, 2188.
[4] Ruff and Keim, *Z. anorg. Chem.*, 1931, **201**, 245; Simons, Bond, and McArthur, *J. Amer. Chem. Soc.*, 1940, **62**, 3477; Simons and Brice, U.S.P. 2,614,131; Haszeldine and Kidd, *J.*, 1953, 3219.
[5] Leech and Burnett, B.P. 633,678; Pennsylvania Salt Manufacturing Co., B.P. 665,253; Burnett, B.P. 676,374; Mantell, Passino, and Teeters, U.S.P. 2,684,987.
[6] Ellis and Musgrave, *J.*, 1950, 3608; 1953, 1063.
[7] Cuthbertson, Holmes, Musgrave, and Tanner, *J. Appl. Chem.*, 1958, **8**, 390.
[8] *E.g.*, Banks, Musgrave, and Sowler, unpublished results quoted in " Advances in Fluorine Chemistry," Vol. I, Butterworths Scientific Publ., London, 1960, p. 23.

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## Experimental

*Materials.*—Chlorine trifluoride, obtained from a commercial cylinder, was passed first through two U-tubes containing sodium fluoride in order to remove hydrogen fluoride [9] and then through a series of traps in which the liquid was fractionally distilled. Methane of 99·8% purity was dried over magnesium perchlorate and was passed through traps at −196° to remove any other condensable impurities. Commercial "oxygen-free" nitrogen was used without further purification.

*Apparatus and Procedure.*—The apparatus consisted essentially of a cylindrical copper reaction vessel, 14·8 cm. long and 6·6 cm. in diameter, which was placed in a water thermostat and was attached to lines for separate admision of the reactants and for withdrawal and analysis of the products. All parts of the system which came into contact with chlorine trifluoride were made of copper, which was freshly reduced before use, and the purification and storage lines for methane and nitrogen were constructed of Pyrex glass. Pressures were measured on Budenberg anti-chlorine metal Bourdon gauges which were not attacked chemically by chlorine trifluoride or by the reaction products.

The normal experimental procedure was to admit a known pressure of chlorine trifluoride to the reaction vessel and then to connect this momentarily to another vessel of known volume filled to a predetermined higher pressure either with pure methane or with a methane–nitrogen mixture. In this way, the required amount of the hydrocarbon could be rapidly added to the halogen fluoride.

Four different methods were used to analyse the reaction mixtures since no one method on its own gave sufficiently detailed information.

(a) *Volumetric analysis.* An aliquot part of an aqueous solution of the products was titrated with sodium hydroxide to determine total hydrogen halides. Another part was treated with an excess of silver nitrate and the remaining silver ions were back-titrated with ammonium thiocyanate; this gave the amount of hydrogen chloride present and hydrogen fluoride was then determined by difference.

(b) *Gas–liquid chromatography.* None of the stationary phases investigated separated completely all the volatile species present unless the excess of hydrogen fluoride and unchanged methane, which tended to overload the column, were first removed. The reaction mixture was therefore condensed in liquid oxygen and any methane was pumped off. Hydrogen fluoride was then absorbed over solid potassium hydroxide, and the remaining products were analysed by gas-chromatography. In some early work, the instrument used had a 12-ft. dinonyl phthalate column and a carbon monoxide flame detector. In later work, the apparatus had a 24-ft. squalane column and was fitted with a katharometer detector.

(c) *Infrared spectroscopy.* The products were introduced into a gas cell with rock-salt windows and analyses were carried out on a double-beam infrared spectrometer, fitted with a rock-salt prism which transmitted in the region 4000—650 cm.$^{-1}$.

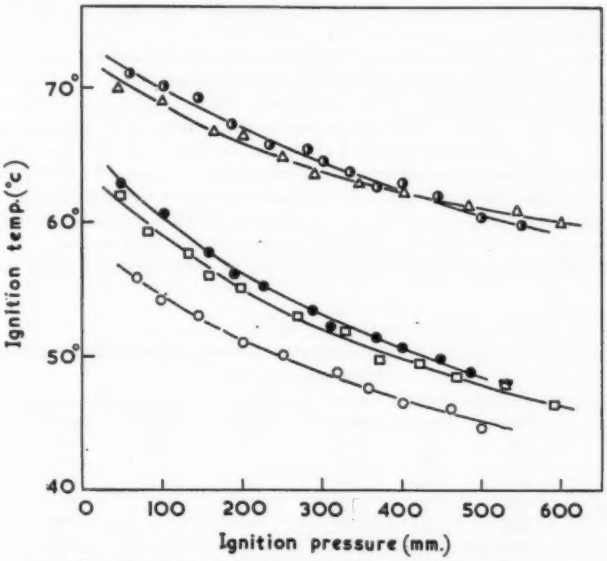
(d) *Nuclear magnetic resonance spectroscopy.* Reaction mixtures were condensed in thick-walled glass tubes, 12 cm. long and 0·3 cm. in diameter, filled to one-quarter of their depth with carbon tetrachloride. The amount introduced was such that at room temperature the total pressure developed was 25—30 atm. The sample tubes were introduced into the metal probe of the spectrometer which contained the radiofrequency source. The probe was placed between the poles of an electromagnet in a position such that the magnetic field over the sample was effectively homogeneous. The radiation used had a frequency of either 40 or 56 mc./sec. and under these conditions hydrogen and fluorine ($^{19}$F) resonances occur at field strengths of about 9346 and 9950 gauss, respectively, so that there was no overlapping of the two spectra. For hydrogen, the maximum range of shifts corresponded to *ca.* 0·3 gauss while for fluorine the range was *ca.* 6 gauss. The various species present were identified from the characteristic resonance line positions which had previously been determined by calibration with pure components. A semiquantitative indication of the concentrations of the products was given by the corrected relative intensities of the resonance lines. However, although the relative amounts of hydrogen- and fluorine-containing constituents may be obtained by comparisons within each separate group of compounds, the results for the two classes cannot be compared with one another. This is due to the fact that the two regions of the resonance spectrum concerned had to be investigated under different conditions of power and sweep rate.

[9] Cf. Banks and Rudge, *J.*, 1950, 191.

## Results

*General Features.*—The influence of pressure and temperature on the ignition limits for a number of chlorine trifluoride–methane mixtures is shown in the Figure. It will be seen that, at a given total pressure, the ignition temperature is lowest for a mixture containing 60% of methane and 40% of chlorine trifluoride.

A striking characteristic of all the systems studied is the extreme suddenness of the transition from immeasurably slow reaction to violent explosion, the change being readily brought about by very small alterations in the experimental conditions. Under conditions near the boundary, explosion was preceded by an appreciable induction period during which there was no detectable consumption of reactants and the length of which was very variable and profoundly affected




Ignition limits for chlorine trifluoride–methane mixtures.

◑ 25% $ClF_3$; □ 33% $ClF_3$; ○ 40% $ClF_3$; ● 50% $ClF_3$; △ 60% $ClF_3$.

by the procedure adopted in the previous run. After explosion, the pressure in the system decreased slowly and often reached eventually a value considerably less than the original reactant pressure.

Packing of the reaction vessel with copper gauze raised the explosion limits to an extent dependent on the resulting surface : volume ratio. As a result of an approximately ten-fold increase in this ratio, the ignition temperature at a given pressure was 10—15° higher (Table 1), but the limits remained as sharp as in an unpacked vessel and no measurable slow reaction could be detected. In the same way, dilution of chlorine trifluoride–methane mixtures with nitrogen also reduced the tendency to explosion, but the suddenness of the transition from negligibly slow to infinitely rapid reaction was little affected.

Table 1.

The influence of the surface on ignition limits of 3 : 2 $CH_4$–$ClF_3$.

| Total pressure (mm.) | 150 | 250 | 400 | 500 |
|---|---|---|---|---|
| Ignition temp.: empty vessel | 53·0° | 50·2° | 46·6° | 44·9° |
| packed vessel | 67·8° | 63·8° | 58·5° | 55·3° |

Since conditions could not be established under which reaction takes place at a conveniently measurable rate, it was not possible to study the kinetics of the slow (non-explosive) reaction in detail. In the circumstances, the only way of deducing something about the sequence of

chemical changes occurring was to construct an artificial picture of the progress of the reaction with time by analysis of the products of the explosive reaction of mixtures containing progressively greater proportions of the halogen fluoride.

*Reaction Products.*—(a) *Qualitative results.* Comparison of the infrared absorption spectra of chlorine trifluoride–methane mixtures with those of the pure reactants and of probable reaction products showed clearly that there was no detectable chemical change under non-explosive conditions. The spectrum of the products of the explosive reaction, although highly complex, yielded some valuable qualitative information. In mixtures containing an excess of methane, considerable amounts of acetylene, ethylene, and ethane were formed and the presence of both fluoro- and chloro-hydrocarbons was suggested by the C–F and C–Cl frequencies observed. On the other hand, after explosion in mixtures containing a large proportion of added nitrogen, no $C_2$ hydrocarbons could be detected and some partially fluorinated methanes appeared to be present.

(b) *Quantitative results.* The presence of hydrogen fluoride (as $SiF_4$) and hydrogen chloride could not be demonstrated spectroscopically owing to the masking effect of certain C–F and C–H bonds in the relevant regions of the spectrum. The extent of formation of these two products was, however, readily obtained by volumetric analysis of aqueous solutions of the reaction products. The results in Table 2 show the amounts of the two acids formed after explosion of mixtures containing an excess of methane. A considerable proportion of the combined fluorine in the chlorine trifluoride is converted into hydrogen fluoride. On the other hand, only a very small proportion of the combined chlorine appears as hydrogen chloride, suggesting that nearly all this halogen in fact becomes organically bound. Results similar to those shown in Table 2 were found for other reactant mixtures and after explosion at 65° and 75°.

TABLE 2.

Formation of hydrogen halides during explosion of methane and chlorine trifluoride at 70°.

| $CH_4$ (mm.) | $ClF_3$ (mm.) | Total acid (mm.) | HCl (mm.) | HF (mm.) | $CH_4$ (mm.) | $ClF_3$ (mm.) | Total acid (mm.) | HCl (mm.) | HF (mm.) |
|---|---|---|---|---|---|---|---|---|---|
| 384 | 128 | 181 | 13 | 168 | 305 | 202 | 148 | 13 | 135 |
| | | 187 | 15 | 172 | | | 148 | 11 | 137 |
| | | 177 | 12 | 165 | | | 150 | 12 | 138 |
| 356 | 178 | 140 | 5 | 135 | 152 | 152 | 209 | 7 | 202 |
| | | 134 | 4 | 130 | | | 212 | 8 | 204 |
| | | 142 | 4 | 138 | | | 200 | 4 | 196 |

TABLE 3.

The relative amounts * of volatile products formed after explosion at 70°, as determined by nuclear magnetic resonance spectroscopy.

Chlorine trifluoride pressure, 100 mm.

| $CH_4$ pressure (mm.) | 100 | 150 | 200 | 300 | $CH_4$ pressure (mm.) | 100 | 150 | 200 | 300 |
|---|---|---|---|---|---|---|---|---|---|
| *Hydrogen-containing products* | | | | | *Fluorine-containing products* | | | | |
| $CH_3Cl$ ..... | (100) | 108 | 118 | 135 | HF ..... | (100) | 99 | 100 | 100 |
| $C_2H_2$ ..... | 34 | 54 | 83 | 128 | $CF_4$ ..... | 11 | 8 | 8 | 6 |
| $C_2H_4$ ..... | 22 | 26 | 31 | 42 | $CF_3Cl$ ..... | 8 | 6 | 6 | 2 |
| $C_2H_6$ ..... | 8 | 10 | 13 | 15 | $CF_2Cl_2$ ..... | 5 | 3 | 4 | 3 |
| $CH_3F$ ..... | 13 | 12 | 10 | 9 | | | | | |

* These are expressed relative to the quantities of methyl chloride and hydrogen fluoride, respectively, formed from an equimolar reactant mixture.

Table 3 gives the amounts of various hydrogen- and fluorine-containing products obtained from the corresponding resonance line intensities; these have been corrected for the numbers of hydrogen and fluorine atoms in the molecules of the various species, so that the figures given represent (within each group) relative molar concentrations. The principal product of the explosive reaction is hydrogen fluoride which is formed together with substantial amounts of methyl chloride, acetylene, and ethylene; smaller quantities of ethane, methyl fluoride, tetrafluoromethane, chlorotrifluoromethane and dichlorodifluoromethane are also present. The

formation of the fully halogenated methanes is inhibited and that of the $C_2$ hydrocarbons is enhanced by the use of mixtures containing initially a high percentage of methane. In the presence of an excess of added nitrogen, the amounts of acetylene and ethylene are markedly reduced and ethane can no longer be detected. At the same time, various partially fluorinated (but no fully fluorinated) methanes were found under these conditions.

Table 4 shows the pressures of the principal organic products formed after explosion of various reactant mixtures. The formation of methyl chloride, acetylene, and ethylene increases and that of the fully halogenated methanes decreases with the proportion of chlorine trifluoride in the initial mixture. Since unchanged methane had to be removed before the other products could be analysed, it was not possible to calculate the proportion of the consumed hydrocarbon

TABLE 4.

The partial pressures of volatile products formed after explosion at 70°, as determined by gas–liquid chromatography.

| | Chlorine trifluoride pressure, 100 mm. | | | |
|---|---|---|---|---|
| $CH_4$ pressure (mm.) | 100 | 150 | 200 | 300 |
| $CH_3Cl$ (mm.) | 2·0 | 2·3 | 3·1 | 5·8 |
| $C_2H_2$ (mm.) | 0·7 | 0·8 | 1·0 | 1·4 |
| $C_2H_4$ (mm.) | 0·5 | 0·6 | 0·7 | 1·2 |
| $CF_4$ (mm.) | 0·9 | 0·7 | 0·3 | 0·1 |
| $CF_3Cl$ (mm.) | 0·6 | 0·3 | 0·4 | 0·2 |
| $CF_2Cl_2$ (mm.) | 0·3 | 0·2 | 0·2 | Trace |

converted into the compounds shown. The yields based on methane initially present can, however, readily be determined and are found to be very low. Thus, on any reasonable assumption of the stoicheiometry of the reaction, it is clear that only a small percentage of the methane used appears as the simple products shown. In conformity with the observation that explosion is generally followed by a decrease in total pressure, the remainder of the consumed hydrocarbon is presumably accounted for mainly by the heavy carbonaceous deposits, which are especially noticeable after explosion of methane-rich mixtures, and to a smaller extent by the polymeric material which is found to contain some fluorine.

## DISCUSSION

Although it was not possible to control the gaseous interaction of chlorine trifluoride with methane and hence study the kinetic features of the slow reaction, the characteristics of the explosive reaction are consistent with a free-radical chain mechanism. Thus the observed sensitivity to the surface conditions of the reaction vessel, the highly variable induction periods, and the extremely sharp explosion limits are all properties which suggest that a chain reaction is in operation.

In the absence of reliable kinetic data, it is impossible to postulate any detailed reaction mechanism, but certain of the analytical results have important implications. In the first place, the fact that the predominant fluorine- and chlorine-containing products are hydrogen fluoride and methyl chloride, respectively, suggests that substitution reactions of the type:

$$Cl{-}F + C{-}H \longrightarrow C{-}Cl + H{-}F$$

are much more widespread than the alternative process:

$$Cl{-}F + C{-}H \longrightarrow C{-}F + H{-}Cl$$

and that the principal action of the halogen fluoride consists in the " stripping off " of hydrogen from the hydrocarbon by fluorine. Secondly, the appearance of relatively large amounts of methyl chloride among the products suggest that this compound is very resistant to attack by chlorine trifluoride, as compared with methane itself. On the other hand, the absence of methyl fluoride and other partially fluorinated compounds from the products of explosion of pure chlorine trifluoride–methane mixtures suggests that these compounds, if formed intermediately, are very rapidly further fluorinated. Only in the presence of an inert gas can the non-stop replacement of hydrogen by fluorine apparently be controlled. Finally, it is clear that the considerable amounts of acetylene, ethylene,

XUM

and ethane formed must arise as a result of the interaction of $C_1$ fragments. Binary recombination of CH, $CH_2$, and $CH_3$ radicals could scarcely account for the extensive formation of the products mentioned and in any case the operation of processes of this kind would be expected to be favoured by added nitrogen, which would tend to act as a third-body. It is more likely that the $C_2$ hydrocarbon products arise from attack by high-energy CH and $CH_2$ radicals on methane itself. There is indirect evidence [10] for the occurrence of reactions of this type and it has been suggested [11] that these radicals are readily deactivated by nitrogen, which would explain the absence of acetylene, ethylene, and ethane in the presence of an excess of an inert gas.

The authors thank Dr. L. Pratt and Dr. D. F. Evans for their help and advice. They also gratefully acknowledge gifts of pure samples of several fluoro- and chlorofluoro-hydrocarbons by the Imperial Smelting Corporation Limited, and of various florube oils and greases by Imperial Chemical Industries Limited, General Chemicals Division, and the loan of two Budenberg anti-chlorine metal Bourdon gauges by the United Kingdom Atomic Energy Authority.

Chemistry Department,
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[10] Kassel, *J. Amer. Chem. Soc.*, 1932, **54**, 3949; Gaydon, *Quart. Rev.*, 1950, **4**, 1.
[11] Arthur, *Nature*, 1950, **165**, 557.

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## 1074. *The Abnormal Hydrolysis of Certain β-(Diarylphosphino)-propionic Esters. Part I.*

By Roy C. Hinton, Frederick G. Mann, and David Todd.

β-(Diphenylphosphino)propionitrile, $Ph_2P{\cdot}[CH_2]_2{\cdot}CN$, on alkaline hydrolysis gives the stable crystalline acid, $Ph_2P{\cdot}[CH_2]_2{\cdot}CO_2H$, but β-(*m*-methoxyphenylphenylphosphino)propionitrile, $m$-$MeO{\cdot}C_6H_4{\cdot}PPh{\cdot}[CH_2]_2{\cdot}CN$, gives *m*-methoxyphenylmethylphenylphosphine, $m$-$MeO{\cdot}C_6H_4{\cdot}PPhMe$. This phosphine is also produced when the corresponding methyl and ethyl propionate are subjected to alkaline or acid hydrolysis.

This " abnormal hydrolysis " is not shown when the ethyl ester is first oxidised to the phosphine oxide, which undergoes alkaline hydrolysis to the stable phosphine oxide carboxylic acid. Replacement of the *m*-methoxyl by the *m*-ethoxyl group in the above phosphine esters also causes hydrolysis to be normal.

Methyl β-(*p*-methoxyphenylphenylphosphino)propionate also undergoes " abnormal hydrolysis," to form *p*-methoxyphenylmethylphenylphosphine, but the replacement of the *p*-methoxyphenyl group by the *p*-ethoxyphenyl group ensures normal hydrolysis.

Production of these tertiary methylphosphines is not caused solely by alkaline or acidic hydrolysis, for the interaction of *m*-methoxyphenylphenylphosphine, $m$-$MeO{\cdot}C_6H_4{\cdot}PPhH$, and methyl acrylate gives the methylphosphine and methyl phosphinopropionate; similarly *p*-methoxyphenylphenylphosphine and ethyl acrylate give the corresponding methylphosphine and the ethyl ester.

Ethyl γ-(*m*-methoxyphenylphenylphosphino)butyrate undergoes normal alkaline hydrolysis

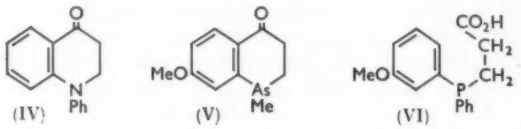
Various aspects of these reactions are discussed.

Crystalline acids of type $Ph_2X{\cdot}CH_2{\cdot}CH_2{\cdot}CO_2H$ can be prepared by alkaline hydrolysis of the nitriles, obtained by the interaction of vinyl cyanide and diphenylamine,[1] diphenylphosphine,[2] and diphenylarsine [3] (I; X = N, P, or As). Whereas, however

[1] R. C. Cookson and Mann, *J.*, 1949, 67.
[2] Mann and Millar, *J.*, 1952, 4453.
[3] R. C. Cookson and Mann, *J.*, 1947, 618.

β-diphenylaminopropionic acid (III; X = N) is cyclised by phosphorus pentoxide in boiling xylene to 1,2,3,4-tetrahydro-4-oxo-1-phenylquinoline [1] (IV), no similar cyclisation of the phosphorus acid [2] (III; X = P) or the arsenic acid (III; X = As) could be achieved, although a wide variety of conditions and reagents was employed.

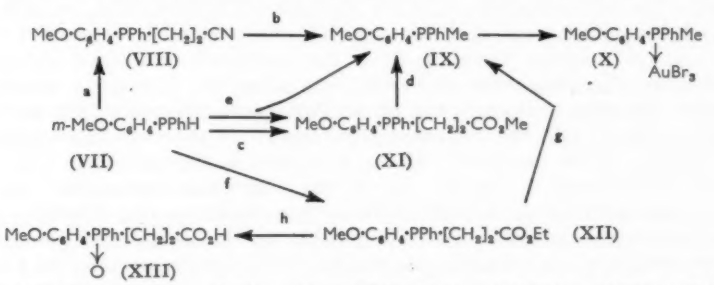
$$Ph_2XH \longrightarrow Ph_2X{\cdot}CH_2{\cdot}CH_2{\cdot}CN \longrightarrow Ph_2X{\cdot}CH_2{\cdot}CH_2{\cdot}CO_2H$$
(I) (II) (III)




In the arsenic series, these difficulties were overcome by the use of the *m*-methoxyphenyl acid, *m*-MeO·$C_6H_4$·AsMe·$[CH_2]_2$·$CO_2H$, cyclisation of which afforded 1,2,3,4-tetrahydro-7-methoxy-1-methyl-4-oxoarsinoline [4] (V).

Since this successful cyclisation was clearly based on the activation of the phenyl group by the methoxyl group (a result also obtained in the indole series),[5] we have attempted to prepare β-(*m*-methoxyphenylphenylphosphino)propionic acid (VI), in order to study its cyclisation, for cyclic oxo-phosphines were unknown when this investigation was started. All our attempts to synthesise the acid (VI) have at present failed, owing to the intervention of an unexpected fission. This paper is primarily a record of our experimental results: a detailed discussion of reaction mechanisms will be deferred until adequate data are available.

*m*-Methoxyphenylphenylphosphine (VII) reacted normally with vinyl cyanide, to give the 2-cyanoethylphosphine (VIII), which, however, when boiled in aqueous-ethanolic sodium hydroxide furnished none of the required acid (VI) but instead afforded *m*-methoxyphenylmethylphenylphosphine (IX). This viscous phosphine was conclusively identified by (i) analysis and molecular-weight determinations; (ii) an independent synthesis in which a solution of the secondary phosphine (VII) in liquid ammonia was treated in turn with one equivalent of sodium and of methyl iodide; (iii) treatment in ethanol with tetrabromoauric acid which gave, by reduction and co-ordination, a colourless aurous bromide




a, $CH_2$:CH·CN. b, EtOH–aq. NaOH. c, Na, Br·$[CH_2]_2$·$CO_2$Me. d, MeOH–aq. NaOH, or dil. HCl.
e, $CH_2$:CH·$CO_2$Me. f, Na, Br$[CH_2]_3$·$CO_2$Et or $CH_2$:CH·$CO_2$Et. g, EtOH–aq. NaOH, or dil. HCl.
h, $H_2O_2$–aq. NaOH.

derivative and thence with one mol. of bromine the highly crystalline orange co-ordinated tribromo-gold derivative (X). The last compound was characterised by analysis and molecular-weight determinations and by its nuclear magnetic resonance spectrum, which showed the presence of MeO· and :PMe groups. Further, the phosphine (IX) showed no

[4] Mann and Wilkinson, *J.*, 1957, 3336.
[5] Mann and Tetlow, *J.*, 1957, 3352.

XUM

phenolic properties: there is therefore no indication that it was the isomeric ethyl-*m*-hydroxyphenylphenylphosphine, which could conceivably have arisen by demethylation and decarboxylation of the required acid (VI). The tribromo-gold compound (X), being readily prepared and purified by recrystallisation, and having a characteristic melting point, was used throughout this investigation as an additional check on the identity of samples of the phosphine (IX). Ethyl-*m*-methoxyphenylphenylphosphine, *m*-MeO·$C_6H_4$·PPhEt, similarly prepared by the action of sodium and ethyl iodide on the phosphine (VII), did not give a well-defined tribromo-gold derivative, but on treatment with a solution of silver iodide in aqueous sodium iodide readily gave a colourless stable compound $(C_{15}H_{17}OP)_2AgI$. The methylphosphine (IX) when similarly treated with silver iodide gave only a gum; with potassium palladobromide it gave a product $[(C_{14}H_{15}OP)_2PdBr_2]$ which after repeated recrystallisation had an indefinite melting point, owing possibly to the presence of racemic and *meso*-forms.

Since the striking difference between the hydrolyses of the unsubstituted nitrile (II; X = P) and its *m*-methoxy-derivative (VIII) might have been caused by the rather vigorous conditions of the hydrolysis, methyl β-(*m*-methoxyphenylphenylphosphino)-propionate (XI) was prepared, to enable milder hydrolysis to be employed. This liquid methyl ester was readily obtained by treating the phosphine (VII) in liquid ammonia with sodium and with methyl β-bromopropionate in turn. When hydrolysed by hot aqueous-ethanolic sodium hydroxide for a brief period, or (more slowly) by boiling 15% hydrochloric acid, it also furnished the phosphine (IX), and the required acid could not be detected.

The methyl ester (XI) was also obtained by heating the phosphine (VII) with pure methyl acrylate under nitrogen, but the crude product, when fractionally distilled, afforded both the ester (XI) and the phosphine (IX). The latter did not apparently arise by thermal decomposition of the former, for this ester was unaffected by being heated under nitrogen in a sealed tube at 100° for 5 hours. The formation of the phosphine (IX) therefore does not necessarily arise solely from a base- or acid-catalysed hydrolytic process.

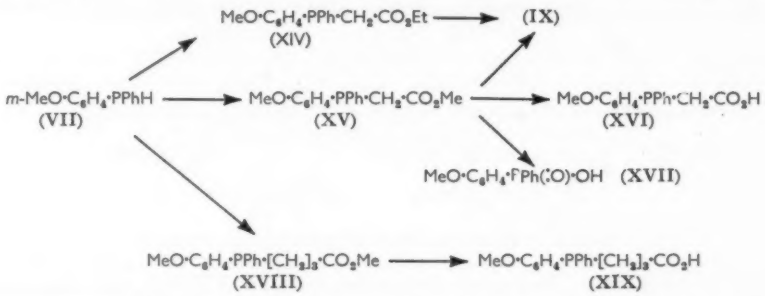
The corresponding ethyl ester (XII) was similarly prepared from the phosphine (VII) both by the reaction of sodium and ethyl β-bromopropionate and by the direct action of pure ethyl acrylate: in neither preparation, however, was the tertiary phosphine (IX) formed as a by-product. However, the ethyl ester (XII), when subjected to the previous alkaline or acidic hydrolysis, also gave the phosphine (IX) as the only volatile product detected. It is significant that when this ester (XII) was oxidised in acetone with hydrogen peroxide, and the resulting phosphine oxide then subjected to alkaline hydrolysis, the stable crystalline phosphine oxide acid (XIII) was obtained. It appears, therefore, that the tervalent phosphorus atom in the nitrile (VIII) and the esters (XI) and (XII) is intimately associated with the " abnormal hydrolysis " to the methylphosphine (IX).

Consideration of the mechanism of the formation of the phosphine (IX) required answers to the following questions: (A) Is the " abnormal hydrolysis " peculiar to β-propionic acid derivatives, or is it shown by homologues having a smaller or larger number of methylene groups? (B) Is it peculiar to the nature and position of the *m*-methoxy-substituent, *i.e.*, would it be shown (i) by the *m*-ethoxy- or (ii) by the *p*-methoxy-analogue?

To obtain evidence regarding factor (A), the *m*-methoxyphenylphenylphosphine (VII) was converted in ammonia by sodium and ethyl chloroacetate into ethyl *m*-methoxy-phenylphenylphosphinoacetate (XIV). This ester proved very resistant to alkaline and acidic hydrolysis, but prolonged boiling with aqueous-ethanolic potassium hydroxide again furnished the methylphosphine (IX). The methyl ester (XV), similarly prepared, readily underwent alkaline hydrolysis to furnish the methylphosphine (IX), the carboxylic acid (XVI) (an oil giving a crystalline benzylthiouronium salt), and *m*-methoxyphenyl-phenylphosphinic acid (XVII). Since the phosphinic acid crystallised only when the initial oil was exposed to air, it is probable that its precursor as the true product of the

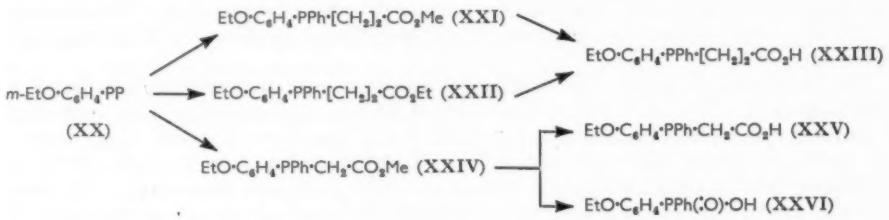
reaction was the corresponding phosphinous acid, $MeO{\cdot}C_6H_4{\cdot}PPh{\cdot}OH$ or the isomeric secondary phosphine oxide, $MeO{\cdot}C_6H_4{\cdot}P(:O)HPh$.

The phosphine (VII), when treated in the usual way with sodium and methyl γ-bromobutyrate, gave the methyl ester (XVIII), which underwent smooth alkaline hydrolysis to




the carboxylic acid (XIX), an oil giving a crystalline benzylthiouronium salt. It appears, therefore, that the "abnormal hydrolysis" does not extend to esters of acids beyond the propionic member.

Question B(i) was clarified by the reactions of *m*-ethoxyphenylphenylphosphine (XX). With methyl acrylate this gave solely the methyl ester (XXI), and with sodium and ethyl β-bromopropionate gave the ethyl ester (XXII). Both products underwent normal alkaline hydrolysis to the acid (XXIII), and there was no evidence of the formation of a neutral tertiary ethoxy-phosphine. The "abnormal hydrolysis," therefore, appears to require specifically the methoxyl group.

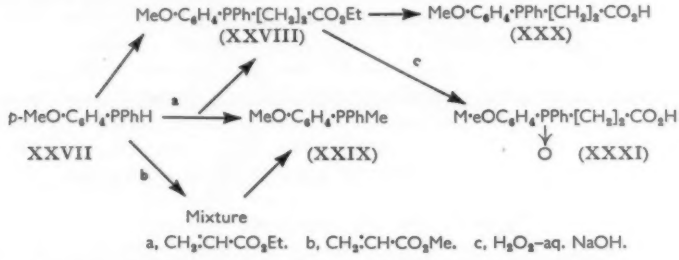



It is noteworthy that the methyl *m*-ethoxyphenylphenylphosphinoacetate (XXIV) on alkaline hydrolysis gave the carboxylic acid (XXV) and the phosphinic acid (XXVI). It is probable that the acid (XXV) was the first product, for longer treatment with the hot aqueous-ethanolic sodium hydroxide decreased the yield of the acid (XXV) and increased that of the acid (XXVI).

To answer the third question, B(ii), analogous reactions were carried out with *p*-methoxyphenylphenylphosphine (XXVII). This phosphine, when treated in liquid ammonia with sodium and ethyl β-bromopropionate, furnished solely ethyl β-(*p*-methoxyphenylphenylphosphino)propionate (XXVIII). When, however, a mixture of the phosphine (XXVII) and pure ethyl acrylate was heated under nitrogen, a mixture of the ethyl ester (XXVIII) and *p*-methoxyphenylmethylphenylphosphine (XXIX) was obtained. The phosphine (XXIX) was identified by its analysis and those of its methiodide and methotoluene-*p*-sulphonate, and by an independent synthesis in which the phosphine (XXVII) in ammonia was treated in turn with sodium and methyl iodide.

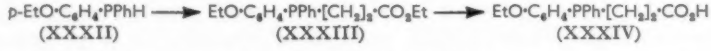
The ethyl ester (XXVIII) when subjected to either mild or vigorous alkaline hydrolysis gave only the corresponding acid (XXX). The stability of this acid under these conditions shows that, in the above interaction of the phosphine (XXVII) and ethyl acrylate, the

methylphosphine (XXIX) must almost certainly have been produced before hydrolysis of the reaction mixture. When the ethyl ester (XXVIII) was oxidised by hydrogen peroxide to the tertiary phosphine oxide, alkaline hydrolysis then afforded the stable phosphine oxide acid (XXXI).




a, $CH_2$:$CH{\cdot}CO_2Et$. b, $CH_2$:$CH{\cdot}CO_2Me$. c, $H_2O_2$–aq. NaOH.

Nevertheless, attempts to prepare the methyl ester (as XXVIII) from the phosphine (XXVII) and (*a*) methyl acrylate or (*b*) sodium and methyl β-bromopropionate gave mixtures. Separation of the components (available in only small amount) was difficult, but in each case the methylphosphine (XXIX) was isolated after alkaline hydrolysis of the mixture. Thus " abnormal hydrolysis " occurs also when the methoxyl group is in the *para*-position, but far less readily than when it is in the *meta*-position.



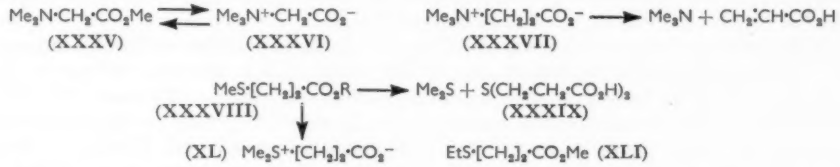

Finally, the *p*-ethoxyphenylphenylphosphine (XXII) with ethyl acrylate gave the ethyl ester (XXXIII), which on hydrolysis furnished the carboxylic acid (XXXIV), an oil which gave a crystalline benzylthiouronium salt. No evidence of the formation of a neutral tertiary phosphine analogous to the *p*-methoxy-phosphine (XXIX) could be obtained.

In considering the possible mechanism by which the *m*-methoxyphenylmethylphenylphosphine (IX) is formed, it should be noted that the hydrolysis of methyl (XV) and ethyl *m*-methoxyphenylphenylphosphinoacetate (XIV) may constitute a special case, because the methylphosphine (IX) may arise by simple decarboxylation of the acid (XVI), a mechanism which could not apply in hydrolysis of the analogous propionates. If therefore the special case of these acetates is excluded, the mechanism for the formation of the methylphosphine (IX) must explain the following facts: (1) The side chain of the hydrolysed compound must be a β-substituted propionic ester or nitrile. (2) The β-phosphorus atom must be present as a tertiary phosphine and not as a tertiary phosphine oxide. (3) The only known substituent required in the phenyl group is a methoxyl group: this group when in the *meta*- or *para*-position promotes " abnormal hydrolysis," but the stronger (or more rapid) effect comes from the *meta*-position. (4) Replacement of the methoxyl group in either position by ethoxyl suppresses " abnormal hydrolysis." (5) The formation of the methylphosphine (IX) occurs in basic aqueous ethanol or in dilute hydrochloric acid, but also occurs when the secondary phosphine (VII) is heated with methyl acrylate in the absence of a solvent or any other reagent: the presence of $H^+$ or $OH^-$ ions is therefore not essential.

Two series of reactions, in the nitrogen and sulphur series respectively, appeared initially to be analogous to our results in the phosphorus series. Willstätter showed that methyl dimethylaminoacetate (XXXV) and trimethylacetobetaine (XXXVI) undergo interconversion, and that heating the propiobetaine (XXXVII) gives mainly trimethylamine and acrylic acid.[6]

[6] Willstätter, *Ber.*, 1902, **35**, 584; Willstätter and Kahn, *Ber.*, 1904, **37**, 401, 1853.

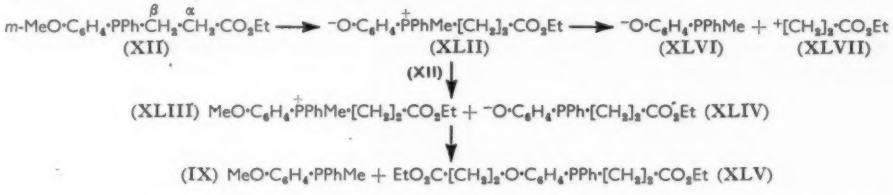
Barger and Coyne [7] showed that ethyl β-(methylthio)propionate (XXXVIII; R = Et) undergoes normal hydrolysis by boiling N-hydrochloric acid to the acid (XXXVIII; R = H), but Challenger and Hollingworth [8] showed that the methyl ester (XXXVIII; R = Me) when boiled with 6N-hydrochloric acid gives dimethyl sulphide and bis-2-carboxyethyl sulphide (XXXIX). The plausible explanation that this "abnormal




hydrolysis" occurs through the intermediate formation of the thetine (XL) or its hydrochloride was refuted * by Challenger *et al.*,[8] who showed that the ethyl ester (XXXVIII; R = Et) when similarly treated also gives dimethyl sulphide, whilst methyl β-(ethylthio)-propionate (XLI) gives diethyl sulphide: neither ester furnishes ethyl methyl sulphide.

Neither the more detailed and complex mechanism suggested by Challenger *et al.*[8] for the abnormal hydrolysis of their sulphur compounds, nor Willstätter's simple mechanism for the nitrogen compounds can apply to our phosphorus compounds, for the methylphosphine (IX) was produced from the nitrile (VIII) and the methyl and ethyl esters (XI, XII), and the hydrolysis of the first and the last of these derivatives was conducted in the absence of any methyl group except that in the *m*-methoxyphenyl unit.

Our results initially appeared to indicate that during the hydrolysis of our nitrile and esters, *e.g.*, the ethyl ester (XII), the propionic acid chain underwent fission between the α- and the β-carbon atom, with formation of the methylphosphine (IX). This mechanism was discarded because (i) the mother liquor from the acidic hydrolysis of the ester (XII) was carefully but fruitlessly examined for aliphatic acids, such as glycollic acid, which might be formed from the α-portion by this process, (ii) if this fission, in spite of its intrinsic improbability, did occur under the influence of the methoxyl group, it should also occur with the corresponding ethoxy-compounds.




We therefore very tentatively suggest that the first stage may be migration of the methyl group in the ester (XII) to the phosphorus atom, to give the phosphonium zwitter-ion (XLII). If this zwitter-ion is an essential intermediate, it would explain (*a*) the stability of the oxidised acid (XIII) which cannot form this type of ion, and (*b*) the fact that abnormal hydrolysis is limited to the methoxy-compounds, for the methyl portion of a methoxyl group has much greater activity than the ethyl portion of an ethoxyl group. The zwitter-ion (XLII) may then react with a second molecule of the ester (XII) to give the *m*-methoxy-cation (XLIII) and the anion (XLIV). The side-arm in the cation (XLIII) will be under strain, however, owing to the opposing electron attractions of the

* In a preliminary note (Hinton, Mann, and Todd, *Proc. Chem. Soc.*, 1959, 365) it was erroneously stated that Challenger *et al.* suggested this mechanism.

[7] Barger and Coyne, *Biochem. J.*, 1928, **22**, 1417.
[8] Challenger and Hollingworth, *Chem. and Ind.*, 1954, 463; *J.*, 1959, 61.

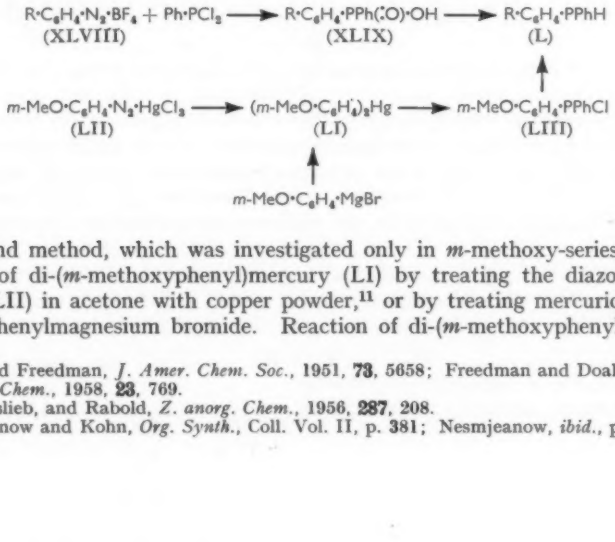
XUM

positive pole and the carbonyl unit: fission may therefore occur between the phosphorus atom and the β-carbon atom, generating the methylphosphine (IX) and the cation (XLVII), which will unite with the anion (XLIV) to give the ether-ester (XLV). Alternatively this overall process might occur by the direct fission of the zwitter-ion (XLII) into the anion (XLVI) and the cation (XLVII): the anion (XLVI) then reacts with the ester (XII) to give the methylphosphine (IX) and the anion (XLIV), which in turn unites with the cation (XLVII) to give the ether-ester (XLV).

If the formation of the zwitter-ion (XLII) is also significantly influenced by the inductive effect of the carboxylic unit, the absence of the " abnormal hydrolysis " when the side-chain extends beyond the propionic member becomes explicable. Moreover, the above reactions may well precede the true hydrolysis, which would apply only to the final ether-ester (XLV). Thus could be formed the methylphosphines (IX and XXIX) by direct action of methyl acrylate on the phosphine (VII), and of ethyl acrylate on the phosphine (XXVII), respectively. Further, a free-radical mechanism parallel to the above ionic mechanism may be involved in these reactions.

Although this mechanism thus provides a tentative explanation of the points (1)—(5) (above), its verification must rest on the isolation of the hydrolysed ether-ester (XLV). In all our distillations of the ether-extracted methylphosphines, a considerable residue of dark, intractable material was obtained. This must now be examined for evidence of the presence of the dicarboxylic acid (as XLV) or any of its likely decomposition products.

*Preparation of Methoxy(and Ethoxy)phenylphenylphosphinic Acids*, $R{\cdot}C_6H_4{\cdot}PPh(:O){\cdot}OH$, *and the Secondary Phosphines*, $R{\cdot}C_6H_4{\cdot}PPhH$.—The preparation of the above *m*- and *p*-methoxy (and ethoxy)phenylphenylphosphinic acids was based on the work of Freedmann and Doak;[9] *m*-methoxyaniline, for example, was converted into the solid diazonium fluoroborate (XLVIII; R = *m*-MeO), which was treated in ethyl acetate suspension with phenylphosphonous chloride and cuprous chloride, subsequent hydrolysis affording the phosphinic acid (XLIX; R = *m*-MeO). The reaction (XLVIII) ⟶ (XLIX) (R = *m*-MeO or *m*-EtO) required very careful control (see Experimental) to ensure a sufficiently vigorous yet not uncontrollably violent reaction: the corresponding reactions of the flouroborates derived from *p*-anisidine and *p*-ethoxyaniline were much less vigorous, and quite mild, respectively. Reduction of the phosphinic acids (XLIX) by lithium aluminium hydride in tetrahydrofuran, instead of ether as recorded [10] for diphenylphosphinic acid, gave the secondary phosphines (L) in very moderate yield: the rather higher yield obtained by converting the acid into its methyl ester before reduction did not, however, justify the extra stage.



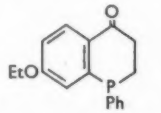

The second method, which was investigated only in *m*-methoxy-series, involved the preparation of di-(*m*-methoxyphenyl)mercury (LI) by treating the diazonium mercury trichloride (LII) in acetone with copper powder,[11] or by treating mercuric chloride with *m*-methoxyphenylmagnesium bromide. Reaction of di-(*m*-methoxyphenyl)mercury (LI)

[9] Doak and Freedman, *J. Amer. Chem. Soc.*, 1951, **73**, 5658; Freedman and Doak, *ibid.*, 1953, **75**, 4905; *J. Org. Chem.*, 1958, **23**, 769.
[10] Hein, Isslieb, and Rabold, *Z. anorg. Chem.*, 1956, **287**, 208.
[11] Nesmejanow and Kohn, *Org. Synth.*, Coll. Vol. II, p. 381; Nesmjeanow, *ibid.*, p. 432.

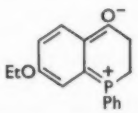
with phenylphosphonous chloride gave only a low yield of rather impure chlorophosphine (LIII), and the reduction of this to the secondary phosphine was also unsatisfactory.

It might appear that all the above difficulties encountered in the synthesis of the acid (VI) might have been evaded by utilising the direct union of the secondary phosphine (VII) and β-propiolactone. However, experiments with diphenylphosphine and the lactone gave none of the corresponding acid, apparently because the secondary phosphine catalyses polymerisation of the lactone too effectively.

Cyclisation of *m*-methoxyphenylphenylphosphino-acetic (XVI) and -butyric acid (XIX), and of *m*-ethoxyphenylpropionic acid (XXIII) has been very briefly investigated. The acids (XVI) and (XIX) when boiled in xylene with phosphorus pentoxide gave only intractable dark gums which did not give 2,4-dinitrophenylhydrazones. The acid (XXIII) gave analogous results when similarly treated in boiling benzene and in xylene, and when




(LIV)




(LIVA)

heated with polyphosphoric acid at 100° for 3 hours was recovered unchanged. A solution of this acid in toluene containing phosphoric anhydride, when boiled for 30 minutes, gave a brown gum which on microdistillation gave a fraction having the composition of the cyclic ketone (LIV): its infrared spectrum had a reasonably strong band at 1720 cm.$^{-1}$, corresponding to a :CO group. The small yield and the difficulty of preparing satisfactory crystalline derivatives caused these attempts to be abandoned: meanwhile the identification of the fraction as the oxo-phosphine (LIV) must be treated with reserve.

It is possible that these failures under conditions of cyclisation that are excellent for the analogous nitrogen acid (III; X = N), may arise largely because the more basic tertiary phosphines form salts with the phosphoric acid: the positive charge on the phosphorus atom would then oppose the activating effect of the *m*-ethoxyl group. The basic properties, moreover, might cause the oxo-phosphine (LIV) to exist mainly as the ionic form (LIVA) and thus increase the difficulty of preparing crystalline derivatives such as hydrazones.

The phosphine oxide propionic acid (XIII) also failed, as expected, to undergo cyclisation under the above conditions or when treated in benzene with phosphorus pentachloride and aluminium chloride in turn: in this acid the phosphorus atom undoubtedly has some positive character.

## Experimental

To ensure consistent m. p.s, certain compounds were heated in evacuated tubes (indicated as E.T.). All compounds were colourless unless otherwise described.

All experiments involving the preparation or subsequent manipulation of secondary or tertiary phosphines were conducted under nitrogen: this is therefore stated later only when particularly necessary.

*Alkaline Hydrolysis.*—For this hydrolysis of the phosphine esters, the following general conditions were observed, unless otherwise stated. A mixture of the ester (*ca.* 5 g.) and 20% aqueous sodium hydroxide (20—25 c.c.) was gently boiled under reflux, and sufficient ethanol (5—8 c.c.) added to give a homogeneous solution, which was boiled for the stated time.

m-*Methoxyphenylphenylphosphinic Acid* (XLIX; R = *m*-MeO).—Concentrated hydrochloric acid (200 c.c.) and *m*-anisidine (120 g.) were added in that order to a stirred solution of sodium fluoroborate (140 g.) in water (400 ml.), which was then cooled whilst a solution of sodium nitrite (68 g., 1·1 mol.) in water (140 c.c.) was added dropwise, so that the temperature remained below 10°. The stirred suspension was then chilled to 0° and the diazonium fluoroborate collected, and washed in turn with aqueous sodium fluoroborate (50 c.c.), methanol (50 c.c.), and with ether (*ca.* 1 l.) until the washings were colourless. The pale brown crystals were spread on drying paper for 1 hr.

A 5-l. round-bottomed flask was fitted with a 3-necked adaptor, the central neck carrying a stirrer, one side-neck being stoppered, and the other carrying a capacious reflux water-condenser, fitted at the top with a wide-bore, inverted U-tube, the open end of which dipped into a large conical overflow flask.

To purify cuprous chloride, it was dissolved in concentrated hydrochloric acid, reprecipitated by the addition of cold boiled water, and then collected, rapidly washed with water and methanol, and dried.

The diazonium fluoroborate was covered with dry ethyl acetate (750 c.c.) in the flask, and then stirred whilst phenylphosphonous chloride (174 g., 1 mol.) was added dropwise, with the intermittent addition of the cuprous chloride (6 g.); the colour of the suspension changed initially from red to brown and became red again when all the phosphine had been added. The flask was then gently warmed by a current of hot water flowing over the shoulders of the flask. After (usually) about 2 hr., a violent reaction started, nitrogen was copiously evolved, and the ethyl acetate began to boil vigorously. Ice-water was then poured copiously over the flask, and the reaction normally subsided at once; occasionally part of the mixture foamed over into the overflow flask, and was later returned to the main reaction mixture. The latter was heated on a boiling-water bath for *ca.* 15 min. and was then cooled, and water (*ca.* 100 c.c.) was cautiously added until hydrolysis was complete.

The ethyl acetate was removed by steam-distillation, and the black oily residual phosphinic acid solidified when cooled. It was purified by digestion with sufficient boiling acetone to dissolve the coloured impurities and most of the phosphinic acid, the latter separating again when the mixture was cooled (yield, 110 g., 46% calc. on the amine used). Recrystallisation from aqueous ethanol gave m-*methoxyphenylphenylphosphinic acid* (XLIX; R = *m*-MeO), m. p. 142—144° (Found: C, 62·7; H, 5·5. $C_{13}H_{13}O_3P$ requires C, 62·9; H, 5·3%). The acid gave a benzylthiouronium salt, m. p. 181—183° after one recrystallisation from water, identical with that prepared from the acid obtained by the hydrolysis of the ester (XV) (see below).

The following points should be noted: (i) to avoid premature decomposition of the fluoroborate, it must be thoroughly washed as described above; (ii) if the phosphonous chloride is added too rapidly, even to a cooled suspension, the fluoroborate may rapidly and vigorously decompose, without forming any phosphinic acid; (iii) the violent reaction described above must be allowed to proceed until the ethyl acetate is boiling vigorously before being cooled: if the reaction is checked prematurely by cooling, the yield of the phosphinic acid may be negligible.

The yield of the phosphinic acid might be increased if the proportion of diazonium fluoroborate were considerably increased:[12] this was not investigated, for the supply of the *m*-anisidine was the determining factor.

m-*Ethoxyphenylphenylphosphinic Acid* (XLIX; R = *m*-EtO).—Unless the conditions given above are carefully followed, the yield of this acid may decrease, even to zero. Although the preparation was carried out on a smaller scale, with pure *m*-phenetidine (80 g.), sodium fluoroborate (90 g.), sodium nitrite (41 g.), phenylphosphonous chloride (121 g., 1 mol.), and cuprous chloride (4 g.), the reaction usually became so violent (after *ca.* 30 minutes' warming) that some of the reaction mixture was blown into the overflow flask. The united mixture was worked up as before, yielding after the first acetone treatment the crystalline *phosphinic acid* (XLIX; R = *m*-EtO) (70 g., 46% calc. on the *m*-phenetidine). The acid usually required 2—3 more treatments with acetone to remove impurities; a sample, recrystallised in turn from acetone, water, and acetone and dried at 100°/0·1 mm., had m. p. 131—134° (E.T.) (Found: C, 64·55; H, 6·1. $C_{14}H_{15}O_3P$ requires C, 64·1; H, 5·8%). It gave a crystalline *benzylthiouronium salt*, m. p. 176°, from water (Found: C, 61·5; H, 6·2. $C_{22}H_{25}N_2O_3PS$ requires C, 61·7; H, 5·9%).

p-*Methoxyphenylphenylphosphinic Acid* (XLIX; R = *p*-MeO).—This was prepared as the *m*-methoxy-analogue, *p*-anisidine (80 g.) and concentrated hydrochloric acid (150 c.c.) being added to sodium fluoroborate (90 g.) in water (300 c.c.), followed by sodium nitrite (44 g.) in water (90 c.c.). The diazonium fluoroborate suspended in ethyl acetate (300 c.c.) was treated with phenylphosphonous chloride (121 g., 1 mol.) and cuprous chloride (0·5 g.). The moderate reaction started after *ca.* 30 min., and external cooling was not always required. The acetone treatment of the final residue gave the *phosphinic acid* (XLIX; R = *p*-MeO) (99 g., 62%);

[12] Denham and Ingram, *J. Org. Chem.*, 1958, **23**, 1298.

a sample recrystallised from water and then from ethanol formed needles, m. p. 184° (E.T.) (Found: C, 63·0; H, 5·1. $C_{13}H_{13}O_3P$ requires C, 62·9; H, 5·3%). The yield was fairly consistent, unlike that of the two *meta*-substituted acids. In this and the following preparation, a very small amount of the copper catalyst is required (in one preparation of the *p*-methoxyphenyl acid, a piece of copper wire wound around the stirrer proved excellent): for the two *meta*-substituted acids, the stated quantities of cuprous chloride are required.

p-*Ethoxyphenylphenylphosphinic Acid* (XLIX; R = *p*-EtO).—This was prepared by converting *p*-phenetidine (120 g.) as before into the diazonium fluoroborate, which was thoroughly washed, dried, and treated in ethyl acetate (400 ml.) with phenylphosphonous chloride (174 g., 1·1 mol.) and cuprous chloride (0·5 g.). The vigorous reaction started after *ca.* 15 min. and did not require controlling. The black residue solidified on cooling, and direct recrystallisation from acetone gave the *phosphinic acid* (XLIX; R = *p*-EtO) (50 g., 22% calc. on the phenetidine): a sample, recrystallised twice from water and then from acetone, had m. p. 148—149° (E.T.) (Found: C, 64·1; H, 5·8%).

m-*Methoxyphenylphenylphosphine* (VII).—All these reductions were carried out under nitrogen. A suspension of the phosphinic acid (XLIX; R = *m*-MeO) (90 g.) in dry tetrahydrofuran (300 c.c.) was cautiously treated with lithium aluminium hydride (10 g.): the mixture sometimes became deep black at this stage owing to contamination with copper but the final yield was unaffected. When the initial reaction had subsided, the mixture was heated under reflux for 4 hr., then concentrated by distillation, and the cold residue hydrolysed with undried ether (*ca.* 500 c.c.), followed by 20% aqueous potassium sodium tartrate (*ca.* 300 c.c.). After the solvent had been removed from the dried ethereal layer, distillation gave the *phosphine* (VII) (13 g., 17%), b. p. 135—140°/0·5 mm. (Found: C, 72·5; H, 6·4. $C_{13}H_{13}OP$ requires C, 72·2; H, 6·1%).

m-*Ethoxyphenylphenylphosphine* (XX).—This was prepared from the phosphinic acid (XLIX; R = *m*-EtO) (90 g.) in the same way as the *m*-methoxy-analogue, but with heating under reflux for 6 hr. The *phosphine* (18 g., 23%) had b. p. 135—136°/0·5 mm. (Found: C, 71·8; H, 6·4. $C_{14}H_{15}OP$ requires C, 73·0; H, 6·6%).

p-*Methoxyphenylphenylphosphine* (XXVII), similarly obtained (12·8 g., 15%) from the phosphinic acid (XLIX; R = *p*-MeO) (98 g.), had b. p. 122—130°/0·5 mm., m. p. 15—16° (Found: C, 71·95; H, 6·2%).

p-*Ethoxyphenylphenylphosphine* (XXXII), similarly prepared from the phosphinic acid (XLIX; R = *p*-EtO) (50 g.), was isolated as a liquid (5·7 g., 13%), b. p. 140—150°/0·8 mm. (Found: C, 72·7; H, 6·7%).

*Di*-(m-*methoxyphenyl*)*mercury* (LI).—(*A*) *m*-Anisidine (54·4 g.) was dissolved in a warm stirred mixture of concentrated hydrochloric acid (250 c.c.) and water (250 c.c.), which on cooling deposited fine crystals of the amine hydrochloride. The mixture was vigorously stirred and cooled in ice–salt whilst powdered sodium nitrite (30 g.) was added during 45 min., ice being added when necessary to keep the temperature at 5—6°. A solution of mercuric chloride (119 g.) in concentrated hydrochloric acid (140 c.c.), mixed with ice (140 g.), was slowly added to the diazonium solution, the temperature being kept at 0°. Vigorous stirring was required as the heavy diazonium mercury trichloride (LII) was deposited. The complete mixture was stirred for 30 min., then filtered at the pump, the trichloride being washed with ice-water (2 × 100 c.c.) and ice-cold acetone (2 × 125 c.c.). The product, dried in a vacuum for 1 hr., afforded orange-brown crystals (68·5 g.). This material, as soon as it was dry, was suspended in acetone (300 c.c.), which was cooled in ice-water and vigorously stirred whilst fine copper powder (59 g.) was added during 30 min. The mixture was stirred for 3 hr., then treated with aqueous ammonia (*d* 0·880; 500 c.c.) and set aside overnight. The product was collected, washed in turn with water and ethanol, and extracted with boiling chloroform. The hot extract was filtered, concentrated, diluted with an equal volume of ethanol, and cooled. *Di*-(m-*methoxyphenyl*)*mercury* (20 g., 22% yield from the *m*-anisidine) which had separated had m. p. 165—167°, raised to 167—168° by recrystallisation from chloroform (Found: C, 40·2; H, 3·7. $C_{14}H_{14}HgO_2$ requires C, 40·5; H, 3·4%).

(*B*) A Grignard reagent was prepared by the interaction of activated magnesium (4·48 g.) in ether (100 c.c.) and *m*-bromoanisole (37·7 g., 1 mol.) in ether (50 c.c.), the complete mixture being boiled under reflux for 3 hr. Powdered dry mercuric chloride (22·5 g.) was added in small portions during 1 hr. to the stirred mixture, giving a vigorous reaction: the mixture was then boiled for 3 hr. The cold stirred mixture was treated with N-hydrochloric acid (10 c.c.)

and filtered, the grey solid residue being washed with fresh ether. This material (24 g.) contained *m*-methoxyphenylmercuric chloride. A sample (2·1 g.) was therefore purified by boiling it in 95% ethanol (100 c.c.) containing sodium iodide (7·5 g.) for 1 hr.;[13] the solution, on cooling, deposited di-(*m*-methoxyphenyl)mercury (1·3 g.), m. p. and mixed m. p. 164—167°. The total yield was 9 g.; some material had been expended investigating methods of working up.

*Chloro*-m-*methoxyphenylphenylphosphine* (LIII).—Di-(*m*-methoxyphenyl)mercury (LI) (50·6 g.) and phenylphosphonous chloride (34·2 g.) were thoroughly mixed and heated under nitrogen at 215—220° for 1 hr. Dry sand (20 g.) was stirred into the viscous reaction mixture, which was extracted thoroughly with cold benzene (3 × 100 c.c.). The combined filtered extracts, after removal of the solvent, gave on distillation a main fraction (14·3 g.), b. p. 164°/1·5 mm.; further distillation caused contamination with a dark flocculent material. The fraction was taken up in light petroleum (b. p. 80—100°; 100 c.c.), which was rapidly filtered; the solvent was removed and the residue redistilled. The main fraction, of unchanged b. p., was the impure chlorophosphine (LIII) (Found: C, 59·7, 59·3; H, 5·6, 5·95. Calc. for $C_{13}H_{12}ClOP$: C, 62·3; H, 4·3%).

Reduction of this compound by lithium aluminium hydride gave the crude phosphine (VII) in low yield, and this route was not further investigated.

m-*Methoxyphenylmethylphenylphosphine*[14] (IX).—*m*-Methoxyphenylphosphine (VII) (6·4 g.) was added to liquid ammonia (*ca.* 125 c.c.) contained in a well-lagged three-necked flask (250 c.c.) fitted with a stirrer. Sodium pellets (0·7 g., 1 equiv.) were added slowly to the stirred solution which finally (20 min.) became bluish-black. Methyl iodide (4·2 g., 0·86 mol.) in ether (15 c.c.) was added dropwise, the solution becoming pale yellow or almost colourless. Evaporation of the ammonia was then hastened by warming. The residue was treated with cold, freshly boiled water (*ca.* 100 c.c.), and the mixture extracted with ether (50 c.c.). The dried ethereal layer on distillation under nitrogen gave a fraction (4·8 g.), b. p. 130—140°/0·5 mm., which on refractionation gave the *methylphosphine* (IX), b. p. 133°/0·5 mm. (Found: C, 72·7; H, 6·4%; *M*, in freezing benzene, 243. $C_{14}H_{15}OP$ requires C, 73·0; H, 6·6%; *M*, 230).

Tetrabromoauric acid was prepared by adding an excess of aqueous-ethanolic sodium bromide to a similar solution of tetrachloroauric acid. This brown solution was then added dropwise with shaking to a cold ethanolic solution of the phosphine (IX) until the solution just attained a permanent red colour. Bromine in fine drops was carefully added until precipitation of the highly crystalline red *tribromo*-m-*methoxyphenylmethylphenylphosphinegold* (X) was complete: the latter, when collected and recrystallised from methanol, had m. p. 151—152° [Found: C, 25·1; H, 2·6%; *M*, in methylene dichloride solution at 30° (thermister method), 686. $C_{14}H_{15}AuBr_3OP$ requires C, 25·2; H, 2·4%; *M*, 667; on evaporation the methylene dichloride solution deposited the unchanged solute, m. p. 148—148·5°].

Nuclear magnetic resonance spectra of hydrogen nuclei were obtained at 40 Mc. by using a Varian Associates 4300B spectrometer and 12″ electromagnet, with flux stabilisation and sample spinning. Positions of the resonances are quoted as chemical shifts on the tetramethylsilane scale. For a chloroform solution of the compound (X), the solvent band precluded observation of resonance of the aromatic C–H bonds, but the methoxyl groups showed up clearly as a sharp peak at the expected value of $\tau = 5{\cdot}3$, and the PMe groups as a doublet at $\tau = 6{\cdot}5$, with a spacing of 12 c./sec. caused by interaction with the magnetic phosphorus atom of spin ½.

When aqueous-ethanolic tetrachloroauric acid was similarly added to an ethanolic solution of the phosphine (IX) and the orange solution then treated with bromine, the crystalline pale orange *dibromochlorophosphinegold* (as X) was deposited, having m. p. 139° (E.T.) after crystallisation from ethanol (Found: C, 26·7; H, 2·2. $C_{14}H_{15}AuBr_2ClOP$ requires C, 27·0; H, 2·4%).

Aqueous-ethanolic potassium palladobromide, when added to slight excess of the ethanolic phosphine (IX), deposited the *dibromodiphosphinepalladium* initially as a brown gum which after three recrystallisations from ethanol still melted indefinitely below 100° (Found: C, 45·8; H, 3·5. $C_{28}H_{30}Br_2O_2P_2Pd$ requires C, 46·3; H, 4·2%).

Only syrups or gums were obtained by the interaction of the phosphine (IX) with methyl iodide, methyl toluene-*p*-sulphonate, rhombic sulphur in benzene solution, hydrogen peroxide in aqueous acetone, ethanolic chloramine-T, or solutions of cuprous iodide and of silver iodide in aqueous potassium iodide.

[13] Whitmore and Sobatski, *J. Amer. Chem. Soc.*, 1933, **55**, 1128.
[14] Cf. Hitchcock and Mann, *J.*, 1958, 2081.

*Ethyl-*m*-methoxyphenylphenylphosphine.*—This phosphine was prepared as was the methyl analogue (IX), the phosphine (VII) (6·85 g.) in liquid ammonia being treated with sodium (0·7 g.) and ethyl bromide (3·5 g., 0·87 mol.). The residue gave a fraction (5·0 g.), b. p. 133—140°/0·5 mm., which on refractionation gave the pure *ethylphosphine*, b. p. 140°/0·5 mm. (Found: C, 74·0; H, 6·9. $C_{15}H_{17}OP$ requires C, 73·8; H, 7·0%).

No solid co-ordinated derivatives of this phosphine with gold tribromide or palladium dibromide could be isolated. When, however, a mixture of the phosphine and a saturated solution of silver iodide in concentrated aqueous sodium iodide was vigorously shaken, a white gum separated that solidified when kneaded with water, and when then recrystallised from ethanol afforded the *iododiphosphinesilver*, m. p. 114° (E.T.) (Found: C, 49·4; H, 4·7%; *M*, in methylene dichloride solution at 30°, 729, 742. $C_{30}H_{34}AgIO_2P_2$ requires C, 49·8; H, 4·7%; *M*, 723). Cuprous iodide similarly gave a white gum but this did not crystallise.

A solution of the ethylphosphine in aqueous-ethanolic sodium hydroxide was boiled under reflux for 2 hr. The phosphine when recovered gave no crystalline tribromogold derivative and therefore was not contaminated with the methylphosphine (IX): the remote possibility that the ethylphosphine is the immediate precursor of the methylphosphine during alkaline hydrolyses of the propionic esters is thus discounted.

*Reactions of* m-*Methoxyphenylphenylphosphine* (VII).—(A) *Vinyl cyanide.* Freshly distilled vinyl cyanide (2·7 g., 1 mol.) was added dropwise to the phosphine (VII) (11·1 g.) in acetic acid (8 c.c.) under nitrogen. The mixture, which had become hot, was boiled under reflux for 10 min., treated with more vinyl cyanide (2·7 g.), and again boiled for 1 hr. The excess of vinyl cyanide and the acetic acid were then boiled off, and the residue was distilled at 0·35 mm.; a small forerun was followed by the main fraction (7·1 g.), b. p. 158—190°, leaving a considerable undistilled black residue. The distillate on refractionation gave *2-cyanoethyl-*m*-methoxyphenylphenylphosphine* (VIII), b. p. 192—193°/0·35 mm. (Found: C, 71·0; H, 6·3. $C_{16}H_{16}NOP$ requires C, 71·4; H, 6·0%). This phosphine did not give a crystalline gold tribromide derivative.

A solution of the cyano-phosphine in 20% aqueous-ethanolic sodium hydroxide under nitrogen was boiled under reflux until no more ammonia was evolved (*ca.* 7 hr). After the ethanol had been removed, the clear solution when cooled and made faintly acid with 10% hydrochloric acid deposited an oil, which was extracted with ether. The dried extract, after removal of the ether, gave on distillation the methylphosphine (IX), b. p. 125—130°/0·5 mm. (Found: C, 72·5; H, 7·0%). This phosphine, both before and after the distillation, gave the tribromogold derivative (X), m. p. and mixed m. p. 151—152° (E.T.) (Found: C, 25·0; H. 2·0%).

(B) *Methyl acrylate.* The phosphine (VII) (8 g.) was treated under nitrogen dropwise with redistilled methyl acrylate (3·2 g., 1 mol.), with considerable heat evolution. The mixture was heated under reflux for 10 min., treated with more methyl acrylate (4 g.), and then heated for 1 hr. The excess of acrylate was removed and the residue, when fractionally distilled, gave the fractions, (i) b. p. 50—130°/0·06 mm. (2 c.c.), and (ii) b. p. 130—170°/0·06 mm. (10 c.c.). Fraction (i) was chiefly dimerised methyl acrylate. Fraction (ii) on refractionation gave fractions (iia) b. p. 110—158°/0·2 mm. (2 c.c.), and (iib) b. p. 158—172°/0·2 mm. (7 c.c.). Fraction (iia) was mainly the methylphosphine (IX), for it gave in high yield the gold tribromide derivative (X) (Found: C, 25·2; H, 2·1%), m. p. and mixed m. p. 149—150° (E.T.) after recrystallisation from methanol. Fraction (iib) on refractionation gave *methyl* β-(m-*methoxyphenylphenylphosphino)propionate* (XI), b. p. 168—170°/0·2 mm. (Found: C, 67·4; H, 6·1. $C_{17}H_{19}O_3P$ requires C, 67·6; H, 6·3%).

This is a typical experiment, but it must be emphasised that in repetitions of this experiment carried out under apparently identical conditions the ratio of phosphine (IX) to the ester (XI) varied considerably, and the precise factor determining this ratio is still unknown.

(C) *Methyl* β-*bromopropionate.* A solution of the phosphine (VII) (4·8 g.) in liquid ammonia was treated with sodium pellets (0·5 g., 1 equiv.) and with the propionate (3·8 g.). The mixture was worked up as for the phosphine (IX). The residue on distillation gave a fraction, b. p. 133—172°/0·2 mm., which on refractionation furnished the methyl ester (XI) (2·0 g.), b. p. 156—165°/0·1 mm. (Found: C, 67·7; H, 6·0%). The methyl ester (XI), treated with tetrabromoauric acid and with bromine, as for (X), gave the *phosphinopropionate tribromogold* (as X), red crystals, m. p. 94—95° (E.T.), from ethanol (Found: C, 27·4; H, 2·7. $C_{17}H_{19}AuBr_3O_3P$ requires C, 27·6; H, 2·6%); the crystals decomposed at room temperature within 24 hr.

The methyl ester was heated under nitrogen in a sealed tube at 100° for 5 hr. It was

recovered unchanged, but now gave a second form of the tribromogold derivative as stable yellowish-orange crystals, m. p. 113° (E.T.) (from methanol) (Found: C, 27·4; H, 2·6%).

The methyl ester (XI) in 20% aqueous-methanolic sodium hydroxide solution was shaken at room temperature for 2 hr. The methanol was boiled off, and the cold aqueous solution made just acid with 10% hydrochloric acid and extracted with ether. Distillation of the dried extract furnished the pure methylphosphine (IX), b. p. 130—140°/0·2 mm. (Found: C, 72·6; H, 6·4%), which gave the tribromogold derivative (X), m. p. and mixed m. p. 149—150° (E.T.) (from methanol) (Found: C, 25·45; H, 2·35%). A considerable dark residue remained undistilled.

A mixture of the ester (XI) and 10% hydrochloric acid was heated in nitrogen under reflux until a clear solution was formed (*ca.* 2 hr.). The cold solution deposited an oil, which was extracted with benzene. The dried extract contained the phosphine (IX), for it readily furnished the tribromogold derivative, m. p. and mixed m. p. 149—150° (E.T.). To identify the other products of hydrolysis, the extracted solution was reduced to small bulk in a vacuum desiccator and then neutralised (phenolphthalein) with aqueous sodium carbonate. This solution, when treated with boiling ethanolic benzylthiouronium chloride, deposited however the *benzylthiouronium salt* of the phosphine oxide propionic acid (XIII), a portion of the acid having undergone oxidation during the working up. The first time this salt was prepared, it had m. p. 125—126° after crystallisation from water: all subsequent preparations gave a salt of m. p. 84° from water (Found, for the high-melting form: C, 60·8; H, 5·6. $C_{24}H_{27}N_2O_4PS$ requires C, 61·25; H, 5·8%). Other components of the extracted solution could not be identified.

(D) *Ethyl acrylate.* Addition of this ester was carried out as that of the methyl ester, but with the phosphine (VII) (10·8 g.) and two additions each of ethyl acrylate (5 g.). The residue on distillation at 0·05 mm. gave fractions, (i) b. p. 65—125° (2 c.c.), and (ii) b. p. 125—190° (13 c.c.). Fraction (i) was mainly polymerised ethyl acrylate. Fraction (ii) on refractionation gave *ethyl* β-(m-*methoxyphenylphenylphosphino*)*propionate* (XII), b. p. 155—158°/0·1 mm. (Found: C, 68·7; H, 6·7. $C_{18}H_{21}O_3P$ requires C, 68·3; H, 6·7%). No methylphosphine (IX) could be detected. The ester (XII) gave a crystalline tribromogold derivative melting below 0°.

(E) *Ethyl* β-*bromopropionate.* This reaction was performed as for the methyl ester, with the phosphine (VII) (12·7 g.), sodium (1·35 g., 1 equiv.), and ethyl β-bromopropionate (10·7 g., 1 mol.). The residue on distillation gave a fraction, b. p. 95—130°/0·015 mm., and an undistilled dark material (3·0 g.). The distillate on refractionation at 0·015 mm. gave the fractions, (i) b. p. 110—115° (2·1 g.), and (ii) b. p. 117—122° (3 g.), and a very small residue. Fraction (ii) was the pure ethyl ester (XII) (Found: C, 68·6; H, 6·8%).

A mixture of the ester and 20% aqueous-ethanolic sodium hydroxide under nitrogen was boiled under reflux for 5 hr. and worked up as before. Distillation of the residue from the ethereal extract gave the methylphosphine (IX), b. p. 115—130°/0·05 mm., identified as the tribromogold derivative (X), m. p. and mixed m. p. 151—152° (E.T.) (Found: C, 25·4; H, 2·5%). The methylphosphine (IX) was also isolated when the cold alkaline solution, after removal of the ethanol, was extracted with benzene.

A mixture of the ester (XII) and 10% hydrochloric acid was boiled under reflux for 4 hr. and worked up as before. The oil, which was extracted with benzene, gave the tribromogold derivative (X), m. p. and mixed m. p. 150—151° (E.T.) (Found: C, 25·3; H, 2·2%).

The ester (0·5 g.) was treated with a solution of hydrogen peroxide (100-vol.; 2 c.c.) in acetone (6 c.c.). When the vigorous reaction had subsided, aqueous sodium hydroxide was added, the acetone distilled off, and then ethanol added to the boiling mixture to give a clear solution, which was boiled under reflux for 6 hr. The ethanol was removed, and the cold solution made almost neutral and extracted with ether to ensure absence of unhydrolysed ester. Acidification of the aqueous solution deposited a white gum, which solidified when rubbed with acetone; recrystallisation from water then gave the *2-carboxyethyl-*(m-*methoxyphenyl*)*phenylphosphine oxide* (XIII), m. p. 153—155° (Found: C, 63·2; H, 5·95%; equiv., 307·5. $C_{16}H_{17}O_4P$ requires C, 63·2; H, 5·6%; equiv., 304).

This acid was also prepared by converting the phosphine (VII) by atmospheric oxidation into the phosphine oxide, which was then mixed with vinyl cyanide (4 mols.) and heated under reflux for 1½ hr. The excess of vinyl cyanide was removed and the gummy residue hydrolysed with aqueous-ethanolic sodium hydroxide. The solution was concentrated, cooled, acidified, and extracted with ether, which when then evaporated left the crystalline acid (XIII), m. p. 153—155·5° after recrystallisation from aqueous methanol (Found: C, 63·0; H, 5·9%).

(F) *Ethyl bromoacetate.* The phosphine (VII) (2·8 g.) was treated in liquid ammonia with sodium (0·3 g.) and ethyl bromoacetate (2·2 g.). The residue when distilled at 0·1 mm. gave a small fore-run and a main fraction (3 g.), b. p. 160—200°: some decomposition appeared to occur during the distillation, leaving much black material. The main fraction when refractionated gave the *ethyl* (m-*methoxyphenylphenylphosphino*)*acetate* (XIV), b. p. 170°/0·1 mm. (Found: C, 67·4; H, 6·5. $C_{17}H_{19}O_3P$ requires C, 67·6; H, 6·3%). This ester did not give crystalline tribromogold or dibromopalladium derivatives. The forerun did not contain the methylphosphine (IX).

A mixture of the phosphine (XIV) and 10% hydrochloric acid, when boiled as before for 12 hr., gave a neutral oily gum, possibly containing unchanged ester. The gum was therefore boiled with aqueous-ethanolic sodium hydroxide for 4 hr. No acidic component could be detected, but the neutral component gave the tribromogold derivative (X), m. p. and mixed m. p. 148·5° (E.T.).

(G) *Methyl bromoacetate.* The phosphine (VII) (10·3 g.) was similarly treated with sodium (1·1 g.) and methyl bromoacetate (7·3 g.). The residue on distillation also gave a small forerun and a main fraction, b. p. 175—220°/0·7 mm. (4·8 g.), which on refractionation gave the pure *methyl ester* (XV), b. p. 176—178°/0·5 mm. (Found: C, 66·95; H, 6·2. $C_{16}H_{17}O_3P$ requires C, 66·65; H, 5·9%). The ester (XV) gave a red *tribromogold derivative*, m. p. 143° (E.T.) (from ethanol) (Found: C, 26·5; H, 2·6. $C_{16}H_{17}AuBr_3O_3P$ requires C, 26·5; H, 2·4%). No unchanged phosphine (VII) could be detected in the small forerun.

The ester (XV) (4·8 g.) was added under nitrogen to 20% aqueous-ethanolic sodium hydroxide, which was boiled under reflux for 4 hr. The ethanol was boiled off, and the clear solution when chilled deposited a small amount of the methylphosphine (IX) as a neutral gum which was extracted with ether and identified as the tribromogold derivative, m. p. and mixed m. p. 148° (E.T.) (from ethanol). The residual aqueous layer when acidified deposited a white gum, which was also isolated by extraction with ether and evaporation of this extract. When the gum was stirred with acetone, the greater part dissolved, leaving crystalline *m*-methoxyphenylphenylphosphinic acid (XVII) (0·3 g.), which had m. p. 144—145° after crystallisation from acetone and then from water (Found: C, 63·3; H, 5·5%). This was confirmed by preparation of the *benzylthiouronium salt*, m. p. 182° (E.T.) (from water) (Found: C, 60·4; H, 5·6; N, 6·9. $C_{31}H_{33}N_2O_3PS$ requires C, 60·8; H, 5·6; N, 6·8%).

The acetone solution of the gum on evaporation gave the syrupy *m*-methoxyphenylphenylphosphinoacetic acid (XVI), identified as the *benzylthiouronium salt*, m. p. 129—130° (E.T.) after two recrystallisations from water (Found: C, 62·7; H, 5·8; N, 6·4. $C_{33}H_{35}N_2O_3PS$ requires C, 62·7; H, 5·7; N, 6·4%). This salt, when treated with hot dilute sulphuric acid, regenerated the acid (XVI) as a gum.

To determine whether the gummy acid (XVI) was readily decarboxylated, it was dissolved in aqueous sodium hydroxide, which was boiled for 1½ hr. The solution when worked up yielded the unchanged acid (XVI), a small quantity of the phosphinic acid (XVII), but none of the methylphosphine (IX). A mixture of the acid (XVI) and 10% hydrochloric acid was therefore boiled for 2 hr., but the mixture on working up gave solely the unchanged acid (XVI), identified as the benzylthiouronium salt, m. p. 125° (E.T.) after one recrystallisation from water.

(H) *Methyl γ-iodobutyrate.* The phosphine (VII) (10·7 g.) was treated in ammonia with sodium (1·14 g.) and with methyl γ-iodobutyrate (11·5 g.). The residue on distillation gave a fraction, b. p. 150—195°/0·15 mm. (8·2 g.), which on refractionation gave *methyl γ-*(m-*methoxyphenylphenylphosphino*)*butyrate* (XVIII), b. p. 172—180°/0·15 mm. (Found: C, 68·25; H, 6·8. $C_{18}H_{21}O_3P$ required C, 68·3; H, 6·7%). No crystalline co-ordinated metallic derivatives could be isolated.

This ester was hydrolysed as before, by 20% aqueous sodium hydroxide to which *ca.* 5% of ethanol had been added, a clear solution being obtained after 1 hour's boiling. On working up as usual, no neutral product could be isolated: acidification gave the acid (XIX) as an oil which gave a crystalline *benzylthiouronium salt*, m. p. 119—120° (E.T.) (from water) (Found: C, 63·7; H, 6·65; N, 6·3. $C_{25}H_{28}N_2O_3PS$ requires C, 64·1; H, 6·2; N, 6·0%). The salt was apparently stable to atmospheric oxidation, but the oily free acid, when treated with hydrogen peroxide in acetone, gave the phosphine oxide which did not apparently give a thiouronium salt.

*Reactions of* m-*Ethoxyphenylphenylphosphine* (XX).—(A) *Ethyl β-bromopropionate.* The

phosphine (XX) (8·9 g.) was treated as usual with sodium (0·9 g.) and ethyl β-bromopropionate (7·0), and the residue on distillation gave *ethyl* β-(m-*ethoxyphenylphenylphosphino*)*propionate* (XXII) (6·7 g.), b. p. >250°/0·5 mm. (Found: C, 69·3; H, 6·9. $C_{19}H_{23}O_3P$ requires C, 69·1; H, 7·0%). Undistilled residue was very small. The ester gave a tribromogold derivative which did not crystallise.

The ester (XXII) (6·7 g.) in aqueous-ethanolic sodium hydroxide was boiled for 1½ hr., the ethanol was removed, and the chilled, clear solution was extracted with ether. No neutral product was isolated from the extract. The aqueous solution when acidified deposited an oil which was extracted with ether: the dried extract when evaporated left the β-(m-*ethoxyphenylphenylphosphino*)*propionic acid* (XXIII) as a gum (5·3 g.) which quickly solidified. For purification, water was added dropwise to a hot ethanolic solution of the acid to produce a faint turbidity: the solution was filtered hot, and when cooled deposited the acid, m. p. 95—95·5° (E.T., shrinks from 90°) (Found: C, 67·2; H, 6·3%; equiv., 295, 298·5. $C_{17}H_{19}O_3P$ requires C, 67·0; H, 6·3%; equiv., 302·5). The acid showed no signs of atmospheric oxidation. It gave a crystalline *benzylthiouronium salt*, m. p. 130—131° (E.T.) (from water) (Found: C, 63·6; H, 6·0; N, 6·3. $C_{25}H_{29}N_2O_3PS$ requires C, 64·1; H, 6·2; N, 6·0%).

(B) *Methyl acrylate.* When the phosphine (XX) (12·8 g.) was added under nitrogen to freshly distilled methyl acrylate (4·8 g., 1 mol.), no heat was evolved. The mixture was boiled under reflux for 70 min., more acrylate (4·8 g.) being added after the first 10 min. Distillation removed the excess of acrylate and then gave only the *methyl ester* (14·4 g.) (XXI), b. p. 178—185°/0·2 mm. (Found: C, 68·3; H, 6·8. $C_{18}H_{21}O_3P$ requires C, 68·3; H, 6·7%).

The methyl ester (XXI) (14·4 g.), when hydrolysed as was the ethyl ester (XXII), required only 15 minutes' boiling, and when similarly worked up afforded the acid (XXIII) (11·8 g.).

(C) *Methyl bromoacetate.* The phosphine (XX) (10 g.) was treated in ammonia with sodium (1 g.) and methyl bromoacetate (6·7 g.). Distillation of the residue gave a fraction, b. p. 155—175°/0·5 mm. (4·4 g.), and much black residue. The fraction on redistillation gave *methyl* (m-*ethoxyphenylphenylphosphino*)*acetate* (XXIV), b. p. 175°/0·5 mm. (Found: C, 67·8; H, 6·7. $C_{17}H_{19}O_3P$ requires C, 67·5; H, 6·3%).

A mixture of the methyl ester (XXIV) (4·4 g.) and 20% aqueous sodium hydroxide containing 5% of ethanol was boiled under reflux in nitrogen for 2 hr. After removal of the ethanol, the cold solution was extracted with ether: this extract on evaporation left no residue. The aqueous solution was acidified, and the precipitated oily acid extracted with ether: this extract when dried and evaporated gave an oily mixture of the acids (XXV) and (XXVI). A portion of the mixture gave the crystalline *benzylthiouronium salt*, m. p. 134° (E.T.) (from water), of (*m*-ethoxyphenylphenylphosphino)acetic acid (XXV) (Found: C, 63·4; H, 6·0; N, 6·2. $C_{24}H_{27}N_2O_3PS$ requires C, 63·1; H, 6·2; N, 6·2%). The remainder of the mixture was stirred with acetone, and after a short period deposited crystalline *m*-ethoxyphenylphenylphosphinic acid (XXVI) (0·43 g.), m. p. 132—135° (E.T.) after two recrystallisations from acetone (Found: C, 64·1; H, 5·6%): the acid gave a *benzylthiouronium salt*, m. p. 176° (E.T.) (from water) (Found: C, 61·9; H, 6·0; N, 6·7. $C_{22}H_{25}N_2O_3PS$ requires C, 61·7; H, 5·9; N, 6·5%). The initial acetone extract on evaporation gave the oily phosphinoacetic acid (XXV) (2·6 g.).

The acid (XXV) (2·6 g.) in 20% aqueous-ethanolic sodium hydroxide was boiled under reflux in nitrogen for 2 hr.; the solution, worked up as before, gave the phosphinic acid (XXVI) (0·25 g.) and a residue of the unchanged acid (XXV) (1·2 g.).

*Reactions of* p-*Methoxyphenylphenylphosphine* (XXVII).—(A) *Methyl iodide.* This preparation was carried out as was that of the *m*-methoxyphenyl analogue (IX). The phosphine (XXVII) (10·8 g.) in liquid ammonia (125 c.c.) was treated in turn with sodium (1·2 g.) and methyl iodide (7·1 g.). After working up, the residue on distillation gave p-*methoxyphenylmethylphenylphosphine* (XXIX), b. p. 135—138°/0·5 mm. (7 g.), as the sole distillate (Found: C, 73·45; H, 6·45; *M*, in benzene by the thermister method, 222. $C_{14}H_{15}OP$ requires C, 73·0; H, 6·6%; *M*, 230).

It readily gave a gummy *methiodide* which solidified when washed with ether, and after recrystallisation from acetone–methyl iodide had m. p. 135° (E.T., shrinking from 130°) (Found: C, 48·8; H, 4·6. $C_{15}H_{18}IOP$ requires C, 48·4; H, 4·9%). It underwent partial dissociation when recrystallised from acetone alone. The phosphine also gave a *methotoluene*-p-*sulphonate*, m. p. 132° (E.T., shrinks at 127°) (from acetone) (Found: C, 63·5; H, 6·2. $C_{22}H_{25}O_4PS$ requires C, 63·4; H, 6·0%). The phosphine gave a silver iodide complex which readily

dissociated in solution: the tribromogold and the dibromopalladium derivative were too soluble in organic solvents for ready isolation.

(B) *Ethyl bromide.* This preparation was similarly performed with the phosphine (XXVII) (10 g.), sodium (1·1 g.), and ethyl bromide (5·1 g.) in ammonia. It afforded *ethyl*-p-*methoxyphenylphenylphosphine* (8·7 g.), b. p. 125—135°/0·3 mm. (Found: C, 74·1; H, 7·1. $C_{15}H_{17}OP$ requires C, 73·8; H, 7·0%). No crystalline derivatives could be isolated.

(C) *Ethyl β-bromopropionate.* The phosphine (XXVII) (10·9 g.) in ammonia was treated with sodium (1·2 g.) and ethyl β-bromopropionate (9·2 g., 1 mol.). The residue, distilled at 0·5 mm., gave a main fraction (3·3 g.), b. p. 184—200°, which on refractionation gave *ethyl* β-(p-*methoxyphenylphenylphosphino*)*propionate* (XXVIII), b. p. 190°/0·5 mm. (Found: C, 68·3; H, 6·4. $C_{18}H_{21}O_3P$ requires C, 68·3; H, 6·7%).

(D) *Ethyl acrylate.* A mixture of the phosphine (XXVII) (17·6 g.) and freshly distilled ethyl acrylate (12 g., 1 mol.) under nitrogen was gently boiled under reflux for 30 min., more acrylate (6 g.) being added after 10 min. Distillation at 0·5 mm. gave the fractions, (i) b. p. 50—100° (2 c.c.), (ii) b. p. 115—145° (7·8 g.), and (iii) b. p. 150—175° (13·5 g.). Fraction (i) was polymerised ethyl acrylate. Fraction (ii) redistilled steadily over 115—130°/0·3 mm.; a sample of b. p. 125—128° was the pure methylphosphine (XXIX) (Found: C, 73·1; H, 6·8%), and gave the methotoluene-*p*-sulphonate, m. p. and mixed m. p. 133° (E.T., shrinks 130°) (from acetone) (Found: C, 63·6; H, 6·05%). Fraction (iii) on refractionation gave the ethyl ester (XXVIII), b. p. 185°/0·3 mm. (Found: C, 68·0; H, 6·8%). In a second apparently similar experiment, only fraction (iii) was obtained.

Hydrolysis of the Ethyl Ester (XXVIII). A mixture of the ester (6·2 g.) and aqueous-ethanolic sodium hydroxide was boiled under reflux for 3 hr. and, after removal of the ethanol, cooled and just acidified. [The precipitated β-(*p*-methoxyphenylphenylphosphino)propionic acid (XXX) separated initially as an emulsion which redissolved in an excess of hydrochloric acid; but when once the acid had collected in globules it dissolved far more slowly in the hydrochloric acid.] The oily acid was isolated by ether extraction but did not crystallise: it gave the crystalline *benzylthiouronium salt*, m. p. 143° (E.T.) (from water) (Found: C, 63·4; H, 6·4; N, 6·1. $C_{24}H_{27}N_2O_3PS$ requires C, 63·1; H, 6·2; N, 6·2%).

Oxidation of the Ester (XXVIII). An acetone solution of the ester (7·3 g.) was treated dropwise with an acetone solution of an excess of hydrogen peroxide (100-vol.), boiled under reflux for 30 min., and then cooled. The solution was basified with sodium hydroxide, the acetone removed, and the boiling continued for another 30 min.; then the clear, cold solution was extracted with ether. The aqueous solution when acidified deposited 2-*carboxyethyl*-(p-*methoxyphenyl*)*phenylphosphine oxide* (XXXI) (6·3 g.) as a white gum which readily solidified, and was purified by precipitation from an ethanolic solution by ether, followed by recrystallisation from ethanol containing 5% of water: the crystals had m. p. 181—182° (E.T.) (Found: C, 62·95; H, 5·9. $C_{16}H_{17}O_4P$ requires C, 63·2; H, 5·6%). The benzylthiouronium salt was too soluble for ready purification. Alternatively, the oily acid (XXX), obtained by hydrolysis of the ester (XXVIII), when similarly oxidised in acetone gave the acid (XXXI), m. p. 178—181° (E.T.) (from aqueous ethanol) (Found: C, 63·1; H, 6·0%).

(E) *Methyl acrylate.* A mixture of the phosphine (XXVII) (9 g.) and freshly distilled methyl acrylate (3·6 g., 1 mol.) was heated under reflux for 20 min. Distillation at 0·5 mm. gave a very small forerun, b. p. <100°, and a main fraction distilling steadily over a range 130—185° (9 g.). Refractionation gave the same fraction, and analysis of the final portion, b. p. 185°, indicated that it was a mixture of the methylphosphine (XXIX) and the methyl ester (as XXVIII) (Found: C, 70·6; H, 6·6%).

The same mixture was apparently formed when the phosphine (XXVII) (7 g.) in ammonia was treated with sodium (0·75 g.) and methyl β-bromopropionate (5·4 g., 1 mol.). The residue gave one main fraction, a sample, b. p. 175°/0·7 mm., being analysed (Found: C, 69·0; H, 6·6%).

The mixed phosphines (7 g.) in aqueous-ethanolic sodium hydroxide were boiled for 1½ hr., the ethanol removed, and the cold solution carefully neutralised: an oil, which was apparently soluble in acidic and basic solutions, separated and was extracted with ether. The ethereal extract after evaporation gave on distillation the methylphosphine (XXIX), b. p. 140—145°/0·5 mm., in very small yield (Found: C, 72·5; H, 6·55%), and a considerable undistilled residue which could not be identified and presumably arose from the amphoteric material. The phosphine (XXIX) was identified as its methotoluene-*p*-sulphonate, m. p. and mixed m. p. 130° (E.T., shrinks at 125°) (Found: C, 63·6; H, 6·3%).

XUM

*Reactions of* p-*Ethoxyphenylphenylphosphine* (XXXII).—A mixture of the phosphine (XXXII) (5·7 g.) and freshly distilled ethyl acrylate (2·2 g.) was heated under reflux for 30 min., and was then distilled, giving solely the *ethyl* β-(p-*ethoxyphenylphenylphosphino*)*propionate* (XXXIII) (7 g.), b. p. 170—175°/0·5 mm. (Found: C, 69·4; H, 7·3. $C_{19}H_{23}O_3P$ requires C, 69·1; H, 7·0%). No trace of a methylphosphine could be detected.

The ethyl ester (XXXIII) (7 g.) was heated as usual with the sodium hydroxide solution for 30 min., and the cold, clear solution acidified. The deposited oil, isolated by ether extraction, yielded the syrupy phosphinopropionic acid (XXXIV), which gave a *benzylthiouronium salt*, m. p. 151—152° (E.T.) (from water) (Found: C, 63·8; H, 6·2; N, 5·9. $C_{25}H_{29}N_2O_3PS$ requires C, 64·1; H, 6·2; N, 6·0%).

*Methyl* m-*Methoxyphenylphenylphosphinate*.—This ester was prepared to investigate its reduction to the phosphine (VII). A stirred mixture of the acid (XLIX; R = *m*-MeO) (30·8 g.) in benzene (50 c.c.) was treated with phosphorus trichloride (40 c.c.) and phosphorus pentachloride (26·0 g., 1 mol.) and set aside overnight. It was then boiled under reflux for 2 hr., and concentrated under reduced pressure: the residual dark oil on distillation gave the colourless acid chloride (27·8 g., 84%), b. p. 175—178°/0·6 mm. The residue yielded unchanged acid (4·0 g.).

The chloride was poured cautiously into a solution of methanol (20 c.c.) in benzene (50 c.c.) at 0°; the mixture was again set aside overnight, and then boiled under reflux for 30 min., and the solvent then removed. The residual oil, which partly crystallised, was dissolved in boiling benzene (*ca.* 75 c.c.), and light petroleum (b. p. 80—100°) (75 c.c.) added. The solution, when cooled in ice, deposited the acid (XLIX; R = *m*-MeO) (9·3 g.), m. p. 136—140°. The filtrate, after extraction with 5% aqueous sodium hydroxide, was dried and distilled, giving the *methyl ester* (15·0 g., 57%), b. p. 183—186°/103 mm., m. p. 45—49° (Found: C, 63·9; H, 5·8. $C_{14}H_{15}O_3P$ requires C, 64·1; H, 5·8%). The acid (9·3 g.) may have been formed by the competing reaction, $R_2P(:O)Cl + MeOH \longrightarrow R_2P(:O)\cdot OH + MeCl$.

Reduction of this ester by lithium aluminium hydride in tetrahydrofuran gave the crude phosphine (VII) in 40—45% yield.

*Methyl* β-(*Diphenylphosphino*)*propionate*.—In early pilot experiments diphenylphosphine and methyl acrylate were combined under nitrogen, initially at room temperature, then heated at 130—140°, to give the *methyl ester*, b. p. 151°/0·4 mm. (Found: C, 70·7; H, 6·5. $C_{16}H_{17}O_2P$ requires C, 70·5; H, 6·3%). It was characterised as the *dibromodi*(*phosphine ester*)*palladium*, golden plates, m. p. 193·5—194·5°, from methanol–benzene (Found: C, 47·1; H, 4·2. $C_{32}H_{34}Br_2O_4P_2Pd$ requires C, 47·4; H, 4·2%).

*Attempted Cyclisation of the Acid* (XXIII).—Some evidence of cyclisation was obtained only under the following conditions. The acid (XXIII) (10·8 g.) was added to a rapidly stirred suspension of phosphorus pentoxide (30 g.) and freshly heated Hyflo Supercel (15 g.) in dry toluene (100 c.c.), which was then boiled under reflux for 30 min. The chilled, pale brown mixture was cautiously hydrolysed with water, made alkaline, and extracted with ether. Evaporation of the dried extract gave a gum, the infrared spectrum of which showed a small peak at 1720 cm.$^{-1}$. The gum, when heated under nitrogen in a sublimation tube at 0·1 mm., afforded a distillate continuously from *ca.* 150—280°, and fractions were collected at *ca.* 50° intervals. The distillates removed at 180° and at 280° showed no peak in the 1720 cm.$^{-1}$ region, whereas that collected at 220° showed a marked peak at this value: a small sample of the distillate at 220—230° appeared to be 7-ethoxy-1,2,3,4-tetrahydro-4-oxo-1-phenylphosphinoline (LIV) (Found: C, 71·4; H, 6·8. Calc. for $C_{17}H_{17}O_2P$: C, 71·8; H, 6·3%). The compound, treated with a solution of silver iodide in saturated aqueous sodium iodide, gave a silver iodide complex, which, after crystallisation from ethanol containing some acetone, had m. p. 120° (E.T.) (Found: C, 38·95; H, 3·3. Calc. for $C_{17}H_{17}AgIO_2P$: C, 39·3; H, 3·3%). This agreement may have been fortuitous, however, for other samples, similarly prepared, had markedly discordant compositions.

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# 1075. *Phosphonitrilic Derivatives. Part IX.*[1] *The Crystal Structure of Octamethylcyclotetraphosphonitrile.*

By Maryon W. Dougill.

The *X*-ray crystal-structure analysis of octamethylcyclotetraphosphonitrile, $[PN(CH_3)_2]_4$, shows that four discrete molecules, with $\bar{4}$ symmetry, crystallise in a tetragonal cell, with dimensions $a = b = 15{\cdot}705$, $c = 6{\cdot}425$ Å, and space group $I4_1/a$. The crystallographically non-equivalent P–N bond lengths are found, by three-dimensional anisotropic refinement, to be equal (1·591 and 1·601 Å; S.D. 0·003 Å). The average P–C bond length is 1·805 Å (S.D. 0·004 Å) and the ring angles are 119° 48′ (∠NPN) and 131° 57′ (∠PNP).

The crystal structures of four phosphonitriles have already been published; three of these are halides[2] and the fourth is the dimethylamide derivative.[3] In each case phosphorus is bonded to an electronegative element and the P–N bond lengths within the ring are short and equal. The actual length depends on the substituent on phosphorus.

The present work was undertaken to provide an accurate structure determination of a simple phosphonitrile containing only light atoms and to observe the structural effect of replacing the strongly electronegative fluorine atom by the isoelectronic methyl group.

There is also interest in the abnormally high melting point of the methyl derivatives;[4] these are 195° and 163° for the trimer and tetramer respectively, whilst the analogous ethyl tetramer is a liquid at room temperature.[5]

## Experimental

Crystals of octamethylcyclotetraphosphonitrile, recrystallised from light petroleum, were kindly prepared by Searle.[4] Small equant crystals of maximum dimension 0·30 mm. were sealed inside a thin-walled glass capillary tube, to prevent hydration.

The photographs were taken at 140° K, by cooling the crystals in a stream of cold, dry nitrogen, in the apparatus described by Robertson.[6] The cell dimensions were obtained from oscillation photographs in the Straumanis position. Multiple-film, equi-inclination Weissenberg photographs of the *a* and *c* axes were recorded for the layers 0*kl* to 10*kl* and *hk*0 to *hk*4. A total of 817 of the possible 886 reflections gave measurable intensities; these were estimated visually by comparison with a calibration strip. Lorentz polarisation factors were calculated and applied on the Leeds University Pegasus computer by a method devised by Dr. F. M. Lovell. No correction was made for absorption.

The three-dimensional refinement was carried out on the Leeds University Pegasus[7] computer by the method of least squares, using the SFLS programme. The scattering factor used for phosphorus was that of Tomiie and Stam,[8] and for carbon, nitrogen, and hydrogen those of Berghuis *et al.*[9] were used; $1/F_0$ was used throughout as the weighting factor.[7] Calculation of the molecular dimensions and analysis of the thermal motion were carried out on the Pegasus computer.[7]

*Crystal Data.*—$[PN(CH_3)_2]_4$, $M = 300{\cdot}2$, m. p. 163°, tetragonal prisms, $a = b = 15{\cdot}705 \pm 0{\cdot}010$, $c = 6{\cdot}425 \pm 0{\cdot}005$ Å, $U = 1584{\cdot}7$ Å$^3$, $D_m = 1{\cdot}19$ g./c.c. (measured by flotation in a liquid in which the crystals are slightly soluble), $Z = 4$, $D_c = 1{\cdot}258$ g./c.c., $F(000) = 640$. Space group $I4_1/a$ ($C_{4h}^6$, No. 88), origin at $\bar{1}$, molecular symmetry $\bar{4}$, Cu-$K_\alpha$ radiation, $\mu = 39{\cdot}4$ cm.$^{-1}$.

[1] Part VIII, Chapman and Paddock, *J.*, in the press.
[2] (*a*) Ketelaar and de Vries, *Rev. Trav. chim.*, 1939, **58**, 1081; (*b*) Wilson and Carroll, *J.*, 1960, 2548; (*c*) McGeachin and Tromans, *J.*, 1961, 4777.
[3] Bullen, *Proc. Chem. Soc.*, 1960, 425.
[4] Searle, *Proc. Chem. Soc.*, 1959, 7.
[5] Bilbo, *Z. Naturforsch.*, 1960, **15***b*, 330.
[6] Robertson, *J. Sci. Instr.*, 1960, **37**, 41.
[7] Cruickshank, Pilling, Bujosa, Lovell, and Truter, "Symposium on Computer Methods," Pergamon Press Ltd., London, 1961.
[8] Tomiie and Stam, *Acta Cryst.*, 1958, **11**, 126.
[9] Berghuis, Haanappel, Potters, Loopstra, MacGillavry, and Veenendall, *Acta Cryst.*, 1955, **8**, 478.

XUM

TABLE 1.

Observed and calculated structure factors (× 10) (Reflections which are too weak to be measured are not included.)

| $\lvert F_o\rvert$ | $F_c$ | $\lvert F_o\rvert$ | $F_c$ | $\lvert F_o\rvert$ | $F_c$ | $\lvert F_o\rvert$ | $F_c$ | $\lvert F_o\rvert$ | $F_c$ | $\lvert F_o\rvert$ | $F_c$ | $\lvert F_o\rvert$ | $F_c$ |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **0,0,*l*** | | **0,15,*l*** | | **1,12,*l*** | | **2,9,*l*** | | **3,6,*l*** | | **4,4,*l*** | | **5,2,*l*** | |
| 4 495 | −481 | 1 164 | 160 | 1 515 | −492 | 1 63 | 38 | 1 736 | −679 | 0 56 | 55 | 1 224 | 235 |
| | | 3 126 | −128 | 3 370 | 369 | 3 375 | −378 | 3 561 | 541 | 2 343 | −303 | 3 786 | −789 |
| **0,1,*l*** | | 5 256 | −249 | 5 167 | 178 | 5 288 | −317 | 5 247 | 232 | 4 330 | −338 | 5 216 | −204 |
| 1 1668 | −1816 | | | | | 7 172 | 184 | 7 210 | −187 | 6 125 | 119 | | |
| 3 664 | −666 | **0,16,*l*** | | **1,13,*l*** | | | | | | | | **5,3,*l*** | |
| 5 82 | 78 | 0 357 | 353 | 2 515 | 522 | **2,10,*l*** | | **3,7,*l*** | | **4,5,*l*** | | 2 811 | −812 |
| 7 46 | 25 | 2 70 | −72 | 4 165 | 160 | 0 551 | 581 | 2 971 | 1003 | 1 106 | −133 | 4 289 | 301 |
| | | 4 383 | −348 | | | 2 398 | −401 | 4 170 | 158 | 3 548 | −550 | 6 128 | 138 |
| **0,2,*l*** | | | | **1,14,*l*** | | 4 191 | −198 | 6 297 | −317 | 5 289 | 342 | | |
| 0 1133 | −1199 | **0,17,*l*** | | | | 6 333 | 325 | | | 7 63 | 56 | **5,4,*l*** | |
| 2 91 | −87 | 1 243 | −266 | 1 115 | 114 | | | **3,8,*l*** | | | | 1 258 | −237 |
| 4 227 | 240 | 3 509 | −456 | 3 96 | 91 | **2,11,*l*** | | | | **4,6,*l*** | | 3 54 | 39 |
| 6 236 | −227 | | | 5 107 | −104 | 1 741 | 707 | 1 741 | 707 | 0 704 | −617 | 5 110 | −122 |
| 8 48 | 46 | **0,18,*l*** | | | | 1 755 | −778 | 5 349 | −362 | 2 67 | −73 | 7 41 | −41 |
| | | | | **1,15,** | | 3 75 | −61 | 7 28 | −32 | 4 802 | 792 | | |
| **0,3,*l*** | | 0 390 | −372 | 2 187 | 183 | 5 223 | 243 | | | 6 18 | −15 | **5,5,*l*** | |
| 1 122 | 116 | 2 198 | −191 | 4 95 | −105 | | | **3,9,*l*** | | | | 2 300 | −298 |
| 3 469 | −456 | | | | | **2,12,*l*** | | | | **4,7,*l*** | | 4 109 | −108 |
| 5 360 | −359 | **0,19,** | | **1,16,*l*** | | 0 983 | −1037 | 2 281 | −275 | | | 6 116 | 125 |
| 7 229 | 216 | 1 140 | 150 | 1 349 | 342 | 2 119 | 131 | 4 235 | −225 | 1 937 | 893 | | |
| | | | | 3 316 | −276 | 4 269 | 282 | 6 62 | 58 | 3 528 | 551 | | |
| **0,4,*l*** | | **0,20,*l*** | | 5 104 | −126 | | | | | 5 347 | −382 | **5,6,*l*** | |
| 0 1764 | −1961 | 0 41 | −35 | | | **2,13,*l*** | | **3,10,*l*** | | 7 63 | −54 | 1 117 | −113 |
| 2 1153 | −1060 | | | **1,17,*l*** | | 1 517 | 546 | 1 150 | 152 | | | 3 467 | 465 |
| 4 477 | 473 | **1,1,*l*** | | | | 3 391 | 396 | 3 316 | −360 | **4,8,*l*** | | 5 322 | 316 |
| 6 218 | 204 | 2 1039 | −1033 | 2 648 | −551 | 5 141 | −163 | 5 61 | −46 | 0 915 | 851 | 7 94 | 91 |
| | | 4 250 | 264 | | | | | | | 2 96 | −101 | | |
| **0,5,*l*** | | 8 145 | −134 | **1,18,*l*** | | **2,14,*l*** | | **3,11,*l*** | | 4 193 | −186 | **5,7,*l*** | |
| 1 321 | 335 | | | 1 339 | −316 | | | 2 804 | −780 | 6 57 | 50 | 2 823 | 825 |
| 3 1171 | 1108 | **1,2,*l*** | | 3 213 | 198 | 0 307 | 292 | 4 36 | 23 | | | 4 207 | −215 |
| 5 44 | −37 | 1 500 | −524 | | | 2 133 | 139 | 6 216 | 192 | **4,9,*l*** | | 6 155 | −163 |
| 7 63 | −66 | 3 216 | 226 | **1,19,*l*** | | 4 190 | −181 | | | 1 278 | −277 | | |
| | | 5 388 | −423 | 2 202 | 215 | | | **3,12,*l*** | | 3 59 | 54 | **5,8,*l*** | |
| **0,6,*l*** | | 7 248 | −226 | | | **2,15,*l*** | | 1 697 | −693 | 5 149 | 167 | 1 278 | 272 |
| 0 1318 | 1325 | | | **2,1,*l*** | | 1 56 | 46 | 3 321 | 345 | 7 141 | −155 | 3 522 | −509 |
| 2 410 | 397 | **1,3,*l*** | | 1 615 | −659 | 3 50 | 28 | 5 230 | 219 | | | 7 83 | 82 |
| 4 245 | −246 | 2 286 | 279 | 3 535 | −552 | 5 50 | −51 | | | **4,10,*l*** | | | |
| 6 110 | 119 | 4 811 | −826 | 5 234 | 236 | | | **3,13,*l*** | | 0 106 | 109 | **5,9,*l*** | |
| | | 8 312 | 318 | 7 168 | −148 | **2,16,*l*** | | 2 730 | 706 | 2 68 | −54 | 2 325 | −324 |
| **0,7,*l*** | | | | | | 0 304 | 300 | 4 66 | −56 | 4 154 | −169 | 4 363 | 385 |
| 1 750 | −763 | **1,4,*l*** | | **2,2,*l*** | | 2 106 | 117 | 6 93 | −103 | 6 358 | −346 | 6 45 | −40 |
| 3 151 | 152 | 1 495 | −478 | 0 56 | 53 | 4 213 | −201 | | | **4,11,*l*** | | | |
| 5 374 | 365 | 3 287 | −268 | 2 411 | −414 | **2,17,*l*** | | **3,14,*l*** | | 1 404 | −404 | **5,10,*l*** | |
| 7 180 | −162 | 5 450 | 417 | 4 107 | 105 | 1 321 | −367 | 1 323 | 315 | 3 351 | −362 | 1 214 | −198 |
| | | 7 293 | 272 | 6 394 | −397 | 3 291 | −288 | 3 160 | −159 | | | 3 328 | 315 |
| **0,8,*l*** | | | | 8 34 | 28 | | | 5 69 | 60 | **4,12,*l*** | | 5 338 | −384 |
| 0 76 | 81 | **1,5,*l*** | | | | **2,18,*l*** | | | | 0 378 | −309 | **5,11,*l*** | |
| 2 658 | 657 | 2 429 | 442 | **2,3,*l*** | | 0 673 | −591 | **3,15,*l*** | | 2 98 | −98 | 4 291 | −296 |
| 4 112 | −124 | 4 326 | 317 | 1 603 | 595 | 2 48 | 45 | 2 88 | 95 | 4 264 | 303 | 6 111 | 108 |
| 6 434 | −440 | 6 73 | 76 | 3 292 | −370 | | | 4 206 | 171 | 6 61 | 70 | | |
| | | 8 70 | −91 | 5 533 | −534 | **2,19,*l*** | | | | | | **5,12,*l*** | |
| **0,9,*l*** | | | | 7 304 | 299 | 1 306 | 331 | **3,16,*l*** | | **4,13,*l*** | | 1 86 | 90 |
| 1 50 | −39 | **1,6,*l*** | | | | | | 1 239 | 244 | 1 113 | 116 | 5 255 | 236 |
| 3 614 | −612 | 1 125 | 111 | **2,4,*l*** | | **2 20*l*,** | | | | 3 188 | 196 | | |
| 5 492 | −496 | 3 171 | 180 | 0 531 | 570 | 0 151 | 177 | **3,17,*l*** | | 5 210 | −210 | **5,13,*l*** | |
| 7 282 | 272 | 5 174 | 175 | 2 542 | −532 | | | 2 398 | −348 | | | 2 50 | −48 |
| | | | | 4 69 | 43 | **3,1,*l*** | | 4 80 | −82 | **4,14,*l*** | | | |
| **0,10,*l*** | | **1,7,*l*** | | 6 557 | 541 | 2 138 | −120 | | | 0 190 | 158 | **5,14,*l*** | |
| 0 449 | −396 | 2 90 | −85 | 8 70 | 91 | 4 114 | −110 | **3,18,*l*** | | 2 47 | −28 | 3 106 | −115 |
| 2 466 | −476 | 4 513 | 533 | | | 6 69 | −62 | 1 287 | −255 | 4 59 | −51 | 5 119 | 127 |
| 4 161 | −162 | 6 61 | −54 | **2,5,*l*** | | 8 128 | −122 | 3 109 | 116 | | | | |
| 6 382 | 388 | | | 1 225 | 199 | | | | | **4,15,*l*** | | **5,15,*l*** | |
| | | **1,8,*l*** | | 3 220 | 275 | **3,2,*l*** | | **3,19,*l*** | | 1 59 | −42 | 4 196 | 178 |
| **0,11,*l*** | | 1 193 | 168 | 5 387 | 367 | 1 926 | 968 | 2 81 | 94 | 3 219 | 217 | | |
| 1 69 | −88 | 3 357 | 354 | 7 91 | −88 | 3 174 | −189 | | | 5 132 | 160 | **5,16,*l*** | |
| 3 138 | 128 | 5 489 | −511 | | | 5 263 | −273 | **4,1,*l*** | | | | 1 84 | −93 |
| 5 44 | 41 | 7 293 | −268 | **2,6,*l*** | | 7 156 | −151 | 1 1415 | 1398 | **4,16,*l*** | | 3 141 | 127 |
| | | | | 0 74 | 51 | | | 3 208 | 196 | 0 83 | −76 | | |
| **0,12,*l*** | | **1,9,*l*** | | 2 145 | −143 | **3,3,*l*** | | 5 209 | −177 | 2 120 | 112 | **5,17,*l*** | |
| 0 521 | −546 | 2 93 | 79 | 4 469 | 468 | 2 661 | −623 | 7 173 | −167 | 4 61 | −48 | 2 225 | 221 |
| 2 112 | 125 | 4 669 | −711 | 6 226 | −218 | 4 492 | −536 | | | | | 4 118 | −140 |
| 4 115 | 109 | 6 33 | −19 | | | 8 323 | 356 | **4,2,*l*** | | **4,17,*l*** | | | |
| 6 261 | 249 | | | **2,7,*l*** | | | | 0 1636 | 1707 | 1 41 | −25 | **5,18,*l*** | |
| | | **1,10,*l*** | | 1 215 | −211 | **3,4,*l*** | | 2 141 | −120 | 3 41 | 23 | 1 198 | 201 |
| **0,13,*l*** | | 1 293 | 277 | 3 548 | 551 | 1 466 | −440 | 4 449 | −455 | | | 3 97 | −123 |
| 1 296 | 319 | 3 687 | −690 | 5 85 | −80 | 3 492 | −474 | 6 141 | −146 | **4,18,*l*** | | | |
| 3 361 | 365 | 5 177 | 200 | 7 146 | −135 | 5 316 | 304 | | | 0 63 | −59 | **5,19,*l*** | |
| 5 361 | 315 | 7 174 | 187 | | | 7 450 | 378 | **4,3,*l*** | | 2 115 | 116 | 2 174 | −233 |
| | | | | **2,8,*l*** | | | | 1 461 | −460 | | | | |
| **0,14,*l*** | | **1,11,*l*** | | 0 144 | 143 | **3,5,*l*** | | 3 423 | −404 | **5,1,*l*** | | **6,1,*l*** | |
| 0 202 | 195 | 2 551 | −540 | 2 392 | 374 | 2 82 | −73 | 5 78 | 82 | 2 1037 | 1035 | | |
| 2 355 | 357 | 4 178 | 178 | 4 187 | −183 | 4 311 | 306 | 7 118 | 111 | 4 326 | −318 | 1 1103 | 1136 |
| 4 45 | 37 | 6 114 | 101 | 6 352 | −368 | 6 219 | 230 | | | 6 190 | −181 | 3 571 | 551 |

TABLE 1. (*Continued.*)

| $\lvert F_o\rvert$ | $F_c$ |
|---|---|
| **6,1,*l*** | |
| 5 342 | −290 |
| 7 132 | −119 |
| **6,2,*l*** | |
| 0 502 | 493 |
| 1 298 | −375 |
| **6,3,*l*** | |
| 1 765 | −769 |
| 3 284 | −291 |
| 5 508 | 492 |
| 7 80 | −72 |
| **6,4,*l*** | |
| 0 172 | −157 |
| 2 521 | 492 |
| 4 183 | 185 |
| 6 260 | −257 |
| **6,5,*l*** | |
| 1 34 | −32 |
| 3 463 | −446 |
| 5 127 | −124 |
| 7 216 | 208 |
| **6,6,*l*** | |
| 0 332 | −325 |
| 4 226 | 228 |
| 6 375 | 375 |
| **6,7,*l*** | |
| 1 664 | 633 |
| 3 54 | 33 |
| 5 62 | −50 |
| 7 104 | −105 |
| **6,8,*l*** | |
| 0 352 | 329 |
| 2 511 | −507 |
| 4 177 | −166 |
| 6 93 | 86 |
| **6,9,*l*** | |
| 1 200 | −196 |
| 3 288 | 286 |
| 5 232 | 247 |
| 7 154 | −249 |
| **6,10,*l*** | |
| 0 166 | −153 |
| 2 421 | 409 |
| 6 475 | −490 |
| **6,11,*l*** | |
| 1 330 | 328 |
| 3 300 | −369 |
| 5 235 | −196 |
| **6,12,*l*** | |
| 0 549 | 548 |
| 2 227 | −220 |
| 4 74 | 67 |
| 6 150 | 170 |
| **6,13,*l*** | |
| 1 416 | −443 |
| 3 150 | −149 |
| 5 89 | 85 |
| **6,14,*l*** | |
| 0 409 | −412 |
| 2 187 | −188 |
| 4 03 | 170 |
| **6,15,*l*** | |
| 1 70 | 63 |
| 3 292 | 244 |
| **6,16,*l*** | |
| 2 76 | 68 |
| **6,17,*l*** | |
| 1 214 | 227 |
| 3 166 | 166 |
| **6,18,*l*** | |
| 0 502 | 493 |
| **7,1,*l*** | |
| 1 393 | −375 |
| **7,2,*l*** | |
| 0 67 | −28 |
| 2 282 | −282 |
| 4 154 | 156 |
| 6 216 | −218 |
| **7,3,*l*** | |
| 1 453 | 444 |
| 3 518 | 534 |
| 5 313 | −291 |
| 7 339 | −309 |
| **7,4,*l*** | |
| 0 145 | 121 |
| 2 460 | 440 |
| 6 382 | −388 |
| **7,5,*l*** | |
| 1 154 | −140 |
| 3 300 | −305 |
| 5 190 | 186 |
| **7,6,** | |
| 2 252 | −259 |
| 4 433 | −429 |
| 6 45 | −4 |
| **7,7,*l*** | |
| 1 459 | −455 |
| 3 113 | −116 |
| 5 291 | 282 |
| 7 39 | 38 |
| **7,9,*l*** | |
| 2 385 | 401 |
| 4 389 | 418 |
| 6 182 | −145 |
| **7,10,*l*** | |
| 1 138 | 149 |
| 3 336 | 335 |
| 5 298 | −343 |
| **7,11,*l*** | |
| 2 358 | 361 |
| 4 252 | −263 |
| **7,12,*l*** | |
| 1 411 | 427 |
| 3 372 | −338 |
| 5 66 | −52 |
| **7,13,*l*** | |
| 2 711 | −735 |
| **7,14,*l*** | |
| 1 442 | −465 |
| 3 256 | 231 |
| 5 174 | 192 |
| **7,15,*l*** | |
| 2 227 | 215 |
| 4 44 | 39 |
| **7,16,*l*** | |
| 1 47 | −50 |
| **7,17,*l*** | |
| 2 372 | 369 |
| **7,18,*l*** | |
| 1 336 | 349 |
| **8,1,*l*** | |
| 1 393 | −357 |
| 3 276 | 268 |
| 5 56 | 40 |
| 7 136 | −127 |
| **8,2,*l*** | |
| 0 733 | −671 |
| 2 326 | 307 |
| 6 63 | 61 |
| **8,3,*l*** | |
| 1 329 | 345 |
| 3 393 | 387 |
| 5 164 | 185 |
| 7 76 | −77 |
| **8,4,*l*** | |
| 0 210 | 196 |
| 2 66 | −39 |
| 4 372 | −385 |
| 6 266 | 294 |
| **8,7,*l*** | |
| 1 452 | −441 |
| 3 495 | −493 |
| 5 284 | 290 |
| 7 81 | −98 |
| **8,8,*l*** | |
| 0 710 | −685 |
| 2 86 | −83 |
| 4 332 | 349 |
| 6 126 | 101 |
| **8,9,*l*** | |
| 1 444 | 449 |
| 3 343 | 360 |
| **8,10,*l*** | |
| 0 155 | 137 |
| 2 109 | 106 |
| 4 132 | −132 |
| 6 78 | −88 |
| **8,11,*l*** | |
| 1 332 | 329 |
| 3 63 | 50 |
| 5 57 | −48 |
| **8,12,*l*** | |
| 0 556 | 561 |
| 4 242 | −225 |
| **8,13,*l*** | |
| 1 387 | −410 |
| 3 386 | −395 |
| 5 166 | 164 |
| **8,14,*l*** | |
| 0 431 | −427 |
| 2 38 | −30 |
| 4 408 | 373 |
| **8,15,*l*** | |
| 1 145 | 143 |
| 3 83 | 87 |
| **8,16,*l*** | |
| 2 166 | −147 |
| **8,17,*l*** | |
| 1 127 | 122 |
| 3 108 | 148 |
| **8,18,*l*** | |
| 0 351 | 343 |
| **9,1,*l*** | |
| 2 304 | −295 |
| 4 481 | 449 |
| 6 57 | −36 |
| **9,2,*l*** | |
| 1 427 | −409 |
| 3 378 | 370 |
| 5 68 | −36 |
| **9,3,*l*** | |
| 2 851 | 822 |
| 4 110 | 107 |
| **9,4,*l*** | |
| 1 463 | 436 |
| 3 76 | −60 |
| 5 338 | −320 |
| 7 187 | −209 |
| **9,5,*l*** | |
| 2 283 | −268 |
| 4 273 | −262 |
| 6 29 | −20 |
| **9,6,*l*** | |
| 1 222 | 211 |
| 3 169 | −163 |
| 5 107 | 99 |
| 7 81 | 105 |
| **9,7,*l*** | |
| 2 762 | −797 |
| 4 87 | 91 |
| 6 89 | 82 |
| **9,8,*l*** | |
| 1 720 | −691 |
| 3 411 | 399 |
| 5 213 | 212 |
| **9,9,*l*** | |
| 2 706 | 718 |
| 6 92 | −89 |
| **9,10,*l*** | |
| 1 255 | 249 |
| 3 387 | −375 |
| 5 85 | −85 |
| **9,11,*l*** | |
| 2 44 | 46 |
| 4 179 | 157 |
| **9,12,*l*** | |
| 1 329 | 344 |
| 3 76 | 62 |
| 5 221 | −204 |
| **9,13,*l*** | |
| 2 382 | −402 |
| 4 188 | −155 |
| **9,14,*l*** | |
| 1 276 | −301 |
| 3 297 | 255 |
| **9,15,*l*** | |
| 2 195 | 168 |
| 4 92 | −101 |
| **9,16,*l*** | |
| 1 117 | −106 |
| 3 210 | −220 |
| **9,17,*l*** | |
| 2 63 | 69 |
| **10,1,*l*** | |
| 1 679 | −683 |
| 3 58 | 24 |
| 5 216 | 209 |
| 7 70 | −79 |
| **10,2,*l*** | |
| 0 1275 | −1265 |
| 2 109 | −131 |
| 4 343 | 333 |
| 6 44 | −30 |
| **10,3,*l*** | |
| 1 849 | 871 |
| 3 769 | 753 |
| 5 216 | −208 |
| **10,4,*l*** | |
| 0 827 | 851 |
| 2 139 | 152 |
| 4 417 | −412 |
| 6 98 | −105 |
| **10,5,*l*** | |
| 1 269 | −245 |
| 3 83 | −73 |
| **10,6,*l*** | |
| 0 402 | 389 |
| 2 283 | 289 |
| 4 71 | −61 |
| 6 57 | −51 |
| **10,7,*l*** | |
| 1 654 | −689 |
| 3 427 | −457 |
| **10,8,*l*** | |
| 0 1226 | −1238 |
| 4 262 | 273 |
| 6 76 | 70 |
| **10,9,*l*** | |
| 1 558 | 567 |
| 3 200 | 209 |
| 5 151 | −126 |
| **10,10,*l*** | |
| 0 369 | 385 |
| 2 248 | −251 |
| 4 233 | −231 |
| **10,11,*l*** | |
| 1 74 | −68 |
| 3 272 | 296 |
| 5 245 | 258 |
| **10,12,*l*** | |
| 0 285 | 270 |
| 2 425 | 460 |
| 4 114 | −102 |
| **10,13,*l*** | |
| 1 57 | 45 |
| 3 369 | −344 |
| **10,14,*l*** | |
| 0 129 | −134 |
| 2 71 | −79 |
| 4 63 | 66 |
| **10,15,*l*** | |
| 3 174 | −160 |
| **10,16,*l*** | |
| 0 211 | −180 |
| 2 243 | −253 |
| **11,1,*l*** | |
| 2 547 | −549 |
| **11,2,*l*** | |
| 1 713 | −756 |
| 3 166 | 163 |
| 5 175 | 179 |
| **11,3,*l*** | |
| 2 849 | 842 |
| 6 121 | −106 |
| **11,4,*l*** | |
| 1 595 | 638 |
| 3 262 | −265 |
| **11,5,*l*** | |
| 2 97 | −95 |
| 4 150 | 152 |
| **11,6,*l*** | |
| 1 227 | 217 |
| 3 171 | 167 |
| 5 171 | −178 |
| **11,7,*l*** | |
| 2 408 | −425 |
| 4 205 | −212 |
| 6 60 | −62 |
| **11,8,*l*** | |
| 1 499 | −527 |
| 3 73 | 74 |
| **11,9,*l*** | |
| 2 177 | 194 |
| 4 116 | −106 |
| **11,10,*l*** | |
| 1 88 | 96 |
| 3 245 | −269 |
| 5 266 | 308 |
| **11,11,*l*** | |
| 4 507 | 459 |
| **11,12,*l*** | |
| 1 158 | 159 |
| 3 337 | 299 |
| **11,13,*l*** | |
| 2 141 | 150 |
| 4 258 | −264 |
| **11,14,*l*** | |
| 1 55 | 65 |
| 3 216 | −196 |
| **11,15,*l*** | |
| 2 215 | −218 |
| **11,16,*l*** | |
| 1 173 | −182 |
| **12,1,*l*** | |
| 1 104 | −105 |
| 3 280 | −251 |
| 5 47 | −32 |
| **12,2,*l*** | |
| 0 301 | −295 |
| 2 350 | −341 |
| 4 271 | 279 |
| 6 148 | 146 |
| **12,3,*l*** | |
| 1 283 | 272 |
| 3 427 | 444 |
| 5 44 | −45 |
| **12,4,*l*** | |
| 0 801 | 779 |
| 2 87 | 96 |
| 4 153 | −161 |
| 6 145 | 174 |
| **12,5,*l*** | |
| 1 173 | −173 |
| 3 73 | 49 |
| 5 187 | 168 |
| **12,6,*l*** | |
| 0 70 | −50 |
| 2 141 | 115 |
| 6 363 | −406 |
| **12,7,*l*** | |
| 1 110 | −107 |
| 3 144 | −138 |
| 5 404 | −372 |
| **12,8,*l*** | |
| 0 320 | −318 |
| 2 121 | −106 |
| 4 89 | −78 |
| **12,9,*l*** | |
| 1 80 | −50 |
| 5 91 | 97 |
| **12,10,*l*** | |
| 2 66 | −51 |
| 4 157 | 140 |
| **12,11,*l*** | |
| 1 89 | −108 |
| 3 320 | 277 |
| **12,12,*l*** | |
| 0 76 | −79 |
| 2 281 | 259 |
| 4 63 | −54 |
| **12,13,*l*** | |
| 1 196 | 233 |
| 3 65 | −59 |
| **12,14,*l*** | |
| 0 287 | 268 |
| 2 46 | −43 |
| **12,15,*l*** | |
| 1 158 | −170 |
| **12,16,*l*** | |
| 0 269 | −272 |
| **13,1,*l*** | |
| 2 89 | −78 |
| 4 421 | −429 |
| 6 86 | 83 |
| **13,2,*l*** | |
| 1 150 | −150 |
| 3 95 | −83 |
| 5 447 | 393 |
| **13,3,*l*** | |
| 2 116 | 111 |
| 4 268 | 264 |
| **13,4,*l*** | |
| 1 108 | 111 |
| 3 76 | −70 |
| 5 72 | 58 |
| **13,5,*l*** | |
| 2 140 | 122 |
| 4 222 | 211 |
| **13,6,*l*** | |
| 1 132 | 126 |
| 3 87 | 89 |
| 5 352 | −333 |
| **13,7,*l*** | |
| 2 76 | 81 |
| 4 417 | −407 |
| **13,8,*l*** | |
| 1 109 | 110 |
| 3 213 | −220 |
| 5 75 | 74 |
| **13,9,*l*** | |
| 2 327 | −377 |
| 4 82 | 68 |
| **13,10,*l*** | |
| 1 310 | −354 |
| 3 240 | 210 |

TABLE 1. (*Continued.*)

| $\lvert F_o\rvert$ | $F_c$ | $\lvert F_o\rvert$ | $F_c$ | $\lvert F_o\rvert$ | $F_c$ | $\lvert F_o\rvert$ | $F_c$ | $\lvert F_o\rvert$ | $F_c$ | $\lvert F_o\rvert$ | $F_c$ | $\lvert F_o\rvert$ | $F_c$ |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **13,11,*l*** | | **14,6,*l*** | | **15,2,*l*** | | **15,10,*l*** | | **16,8,*l*** | | **17,5,*l*** | | **18,5,*l*** | |
| 2 266 | 235 | 0 279 | 286 | 1 70 | 40 | 1 336 | −316 | 0 295 | 299 | 2 255 | 239 | 1 44 | 44 |
| 4 187 | 200 | 2 85 | 75 | 3 231 | −247 | 3 370 | 344 | 2 94 | −84 | 4 44 | −53 | 3 32 | −28 |
| | | 4 83 | −77 | 5 82 | 77 | | | | | | | | |
| **13,12,*l*** | | | | | | **15,11,*l*** | | **16,9,*l*** | | **17,6,*l*** | | **18,6,*l*** | |
| 1 78 | 77 | **14,7,*l*** | | **15,3,*l*** | | 2 316 | 296 | 1 221 | −220 | 1 72 | −70 | 0 196 | −176 |
| | | 1 209 | 211 | | | | | 3 146 | −145 | 3 265 | −267 | 2 164 | −172 |
| **13,13,*l*** | | 5 203 | −229 | 2 430 | −444 | **15,12,*l*** | | | | | | | |
| 2 181 | 187 | | | 4 198 | 174 | 1 97 | 94 | **16,10,*l*** | | **17,8,*l*** | | **18,7,*l*** | |
| | | **14,8,*l*** | | | | | | 0 284 | −243 | 1 148 | 148 | 1 46 | −36 |
| **13,14,*l*** | | | | **15,4,*l*** | | **16,1,*l*** | | 2 104 | 109 | 3 49 | 62 | | |
| 1 313 | 322 | 0 532 | 545 | | | | | | | | | **18,8,*l*** | |
| | | 2 125 | −121 | 1 346 | −358 | 3 187 | −176 | | | | | 0 42 | 31 |
| **14,1,*l*** | | 4 222 | −206 | 3 353 | 327 | | | **16,11,*l*** | | **17,9,*l*** | | | |
| | | | | 5 109 | 139 | **16,2,*l*** | | | | | | **19,1,*l*** | |
| 1 276 | 272 | **14,9,*l*** | | | | | | 1 190 | 204 | 2 32 | −28 | | |
| 3 348 | −343 | 1 454 | −498 | **15,5,*l*** | | 0 54 | 18 | | | | | 2 88 | −93 |
| 5 193 | −179 | 3 202 | −194 | | | 2 38 | −31 | **16,12,*l*** | | **17,10,*l*** | | | |
| | | | | 2 330 | 336 | 4 96 | −86 | | | | | **19,2,*l*** | |
| **14,2,*l*** | | **14,10,*l*** | | 4 44 | 40 | | | 0 102 | 99 | 1 108 | 111 | | |
| | | | | | | **16,3,*l*** | | | | | | 1 150 | 165 |
| 0 325 | 291 | 0 632 | −682 | **15,6,*l*** | | 1 242 | −251 | **17,1,*l*** | | **18,1,*l*** | | | |
| 2 257 | −264 | 2 50 | 25 | | | 3 306 | −261 | | | | | **19,3,*l*** | |
| 4 73 | 70 | 4 287 | 308 | 1 227 | 237 | | | 2 165 | −150 | 1 219 | −221 | | |
| | | | | 3 102 | −90 | **16,4,*l*** | | 4 142 | 139 | 3 121 | 116 | 2 28 | 29 |
| **14,3,*l*** | | **14,11,*l*** | | | | | | | | | | **19,4,*l*** | |
| 1 349 | −354 | 1 178 | 204 | **15,7,*l*** | | 0 508 | −516 | **17,2,*l*** | | **18,2,*l*** | | | |
| 3 76 | −68 | 3 176 | 164 | | | 2 64 | 64 | | | | | 1 50 | −42 |
| 5 291 | 240 | | | 2 112 | 112 | 4 414 | 431 | 1 160 | 180 | 0 80 | 73 | | |
| | | **14 ,12,*l*** | | 4 104 | −103 | | | 3 153 | 123 | 2 357 | 359 | **19,5,*l*** | |
| **14,4,*l*** | | 0 134 | 111 | | | **16,5,*l*** | | | | | | | |
| | | | | **15,8,*l*** | | | | **17,3,*l*** | | **18,3,*l*** | | 2 86 | −121 |
| 0 384 | −398 | | | | | 1 301 | 335 | | | | | | |
| 2 115 | −116 | **14,14,*l*** | | 1 180 | 198 | 3 255 | 228 | 2 297 | −271 | 1 70 | 68 | **19,6,*l*** | |
| 4 250 | 225 | 0 320 | 292 | 3 313 | −285 | | | 4 171 | −171 | 3 215 | −220 | | |
| | | | | | | **16,6,*l*** | | | | | | 1 148 | −206 |
| **14,5,*l*** | | **15,1,*l*** | | **15,9,*l*** | | | | **17,4,*l*** | | **18,4,*l*** | | | |
| | | | | | | 0 345 | 303 | | | | | **20,2,*l*** | |
| 1 213 | 209 | 2 99 | 101 | 2 403 | −385 | 2 86 | −85 | 1 228 | −259 | 0 196 | −162 | | |
| 3 238 | 253 | 4 300 | −273 | 4 57 | 53 | 4 271 | −222 | 3 294 | 279 | 2 44 | −49 | 0 158 | 135 |

TABLE 2.

Atomic co-ordinates in Å ($\sigma$ is the standard deviation in Å).

| | $x$ | $\sigma(x)$ | $y$ | $\sigma(y)$ | $z$ | $\sigma(z)$ |
|---|---|---|---|---|---|---|
| P | 1·7646 | 0·0006 | 2·9019 | 0·0006 | 1·0113 | 0·0008 |
| N | 0·541 | 0·002 | 2·212 | 0·003 | 0·264 | 0·003 |
| $C_1$ | 3·200 | 0·003 | 2·528 | 0·004 | −0·011 | 0·004 |
| $C_2$ | 2·140 | 0·004 | 2·122 | 0·004 | 2·599 | 0·004 |
| $H_1$ | 4·07 | 0·04 | 2·92 | 0·04 | 0·49 | 0·04 |
| $H_2$ | 3·07 | 0·04 | 3·12 | 0·05 | −0·97 | 0·05 |
| $H_3$ | 3·27 | 0·04 | 1·60 | 0·04 | −0·19 | 0·05 |
| $H_4$ | 3·05 | 0·05 | 2·47 | 0·05 | 3·00 | 0·05 |
| $H_5$ | 1·35 | 0·05 | 2·23 | 0·05 | 3·35 | 0·06 |
| $H_6$ | 2·32 | 0·05 | 1·07 | 0·05 | 2·48 | 0·06 |

TABLE 3.

Thermal parameters (units in $10^{-4}$ Å$^2$).

| | $U_{11}$ | $\sigma$ | $U_{22}$ | $\sigma$ | $U_{33}$ | $\sigma$ | $U_{12}$ | $\sigma$ | $U_{13}$ | $\sigma$ | $U_{23}$ | $\sigma$ |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| P | 199 | 3 | 193 | 3 | 294 | 4 | 7 | 4 | −23 | 5 | −67 | 5 |
| N | 191 | 10 | 285 | 12 | 385 | 14 | 23 | 18 | −195 | 21 | −27 | 20 |
| $C_1$ | 234 | 12 | 438 | 18 | 473 | 18 | 6 | 24 | −247 | 30 | −6 | 26 |
| $C_2$ | 513 | 20 | 324 | 16 | 407 | 17 | 10 | 28 | 136 | 28 | −229 | 28 |

| | $U$ | $\sigma$ | | $U$ | $\sigma$ | | $U$ |
|---|---|---|---|---|---|---|---|
| $H_1$ | 157 | 99 | $H_3$ | 170 | 105 | $H_5$ | 375 | 142 |
| $H_2$ | 343 | 135 | $H_4$ | 337 | 144 | $H_6$ | 348 | 142 |

TABLE 4.

Magnitude and direction of the principal axes of the ellipsoids of thermal motion with respect to the crystallographic axes. ($l$, $m$, and $n$ are direction cosines.)

| | Å$^2$ | $l$ | $m$ | $n$ | | Å$^2$ | $l$ | $m$ | $n$ |
|---|---|---|---|---|---|---|---|---|---|
| P | 0·0188 | −0·951 | −0·041 | −0·306 | $C_1$ | 0·0234 | −1·000 | +0·010 | −0·007 |
| | 0·0306 | −0·301 | −0·196 | +0·948 | | 0·0580 | −0·012 | −0·656 | +0·755 |
| | 0·0192 | −0·072 | +0·994 | +0·088 | | 0·0331 | +0·003 | +0·755 | +0·656 |
| N | 0·0190 | −0·995 | +0·101 | −0·018 | $C_2$ | 0·0271 | +0·270 | −0·751 | +0·603 |
| | 0·0446 | −0·069 | −0·521 | +0·851 | | 0·0593 | −0·814 | +0·157 | +0·559 |
| | 0·0226 | +0·077 | +0·848 | +0·525 | | 0·0380 | +0·514 | +0·642 | +0·569 |

### Structure Determination

The position of the phosphorus atom was found from the Patterson synthesis projected down [*c*]. Fourier methods were used to locate the positions of the nitrogen and the carbon atoms; these four atoms (and six hydrogen atoms) in the 16-fold general positions are sufficient to define the structure. Two-dimensional refinement, by alternate structure-factor and difference Fourier calculations, was discontinued at $R(hk0) = 0{\cdot}16$.

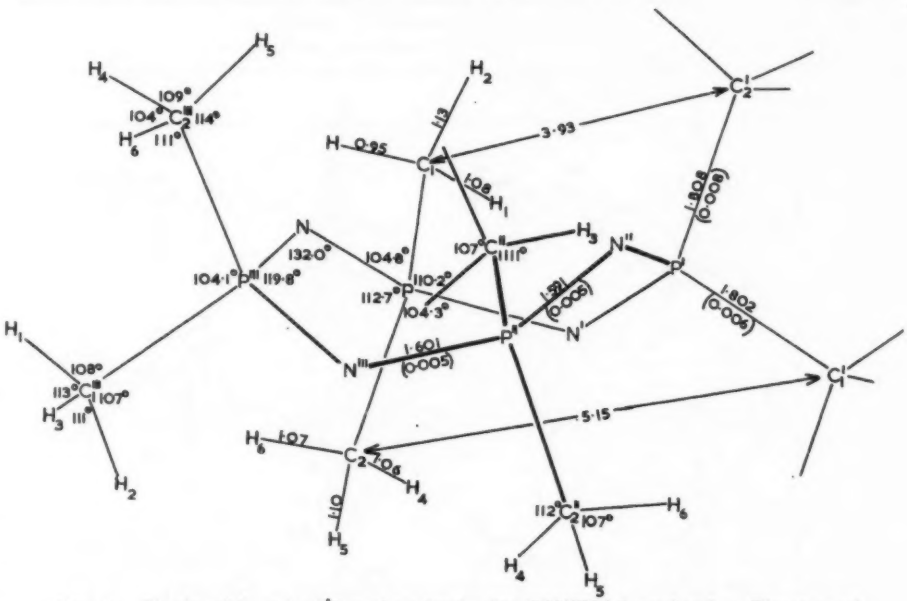



FIG. 1. The bond lengths (Å) and angles in the $[PN(CH_3)_2]_4$ molecule. The sum of the standard deviation and thermal motion correction is shown in Å in parentheses; for the angles at the phosphorus atom this value is 0·2° and 0·3° for the angle NPN'.[10]

The *z*-co-ordinate of the phosphorus atom was obtained from the 0*kl* Patterson synthesis. The *x*, *y*, and *z* parameters were refined simultaneously in this projection to $R(0kl) = 0{\cdot}13$. Individual isotropic temperature factors were applied in the last two calculations.

TABLE 5.

Magnitudes and directions of the principal axes of translational and oscillational ellipsoids.

| Å² | *l* | *m* | *n* | θ | *l* | *m* | *n* |
|---|---|---|---|---|---|---|---|
| 0·0188 | +0·5209 | −0·8536 | −0·0014 | 1·50° | +0·0003 | +0·0001 | +1·0000 |
| 0·0197 | −0·0014 | −0·0006 | +1·0000 | 2·97 | −0·8599 | −0·5105 | +0·0003 |
| 0·0188 | +0·8763 | +0·4818 | +0·0010 | 2·79 | −0·5105 | +0·8599 | +0·0000 |

Corrections to the atomic co-ordinates due to the thermal motion (Å).

| | *x* | *y* | *z* | | *x* | *y* | *z* |
|---|---|---|---|---|---|---|---|
| P ..... | +0·0027 | −0·0017 | +0·0005 | $C_1$ ..... | +0·0044 | −0·0021 | −0·0018 |
| N ..... | +0·0009 | −0·0027 | −0·0013 | $C_2$ ..... | +0·0030 | −0·0027 | +0·0040 |

The initial cycle of three-dimensional refinement was computed with isotropic temperature factors, individual anisotropic temperature factors being used thereafter. During five cycles of refinement, *R* decreased from 0·262 to 0·077. Examination of the low-order reflections revealed that extinction alone could not account for the discrepancy between the observed and

[10] Darlow, *Acta Cryst.*, 1960, **13**, 683.

the calculated structure factors. The contributions of the six hydrogen atoms were consequently included. The hydrogen atoms were placed in the staggered orientation with respect to the other ligands on the phosphorus atom, and the co-ordinates were chosen to make the C–H bond length equal to 1·09 Å. An isotropic temperature factor corresponding to a mean-square amplitude of vibration of 0·06 Å was used. After three further cycles, in which all the atoms were allowed to move, a final $R$ of 0·057 was obtained (observed reflections only). The refinement was judged to be complete when the shifts in the atoms, excluding hydrogen

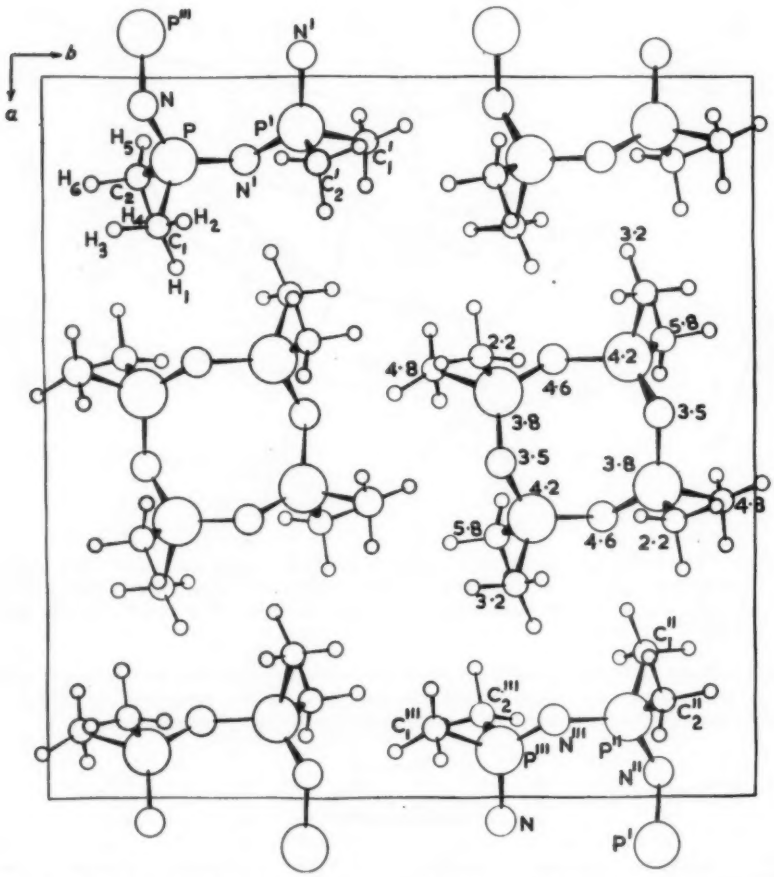
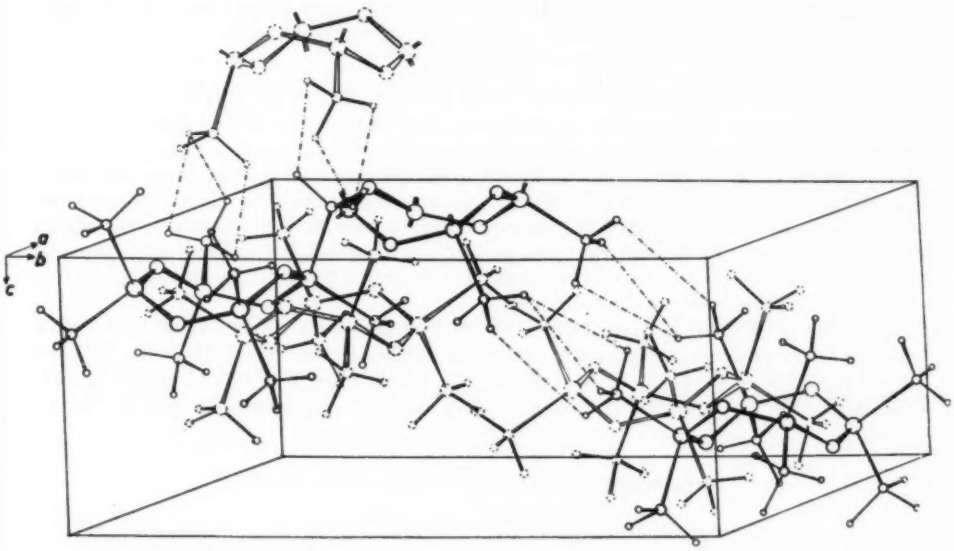



FIG. 2. Projection of the structure down the $c$ axis. The heights of the atoms are in Å.

atoms, were less than one-third of their estimated standard deviation. The validity of the hydrogen atom co-ordinates is indicated by the decrease of their thermal motion during the refinement (Table 3).

*Results.*—A list of observed and calculated structure factors for the observed reflections is given in Table 1. The final atomic co-ordinates with their standard deviations are given in Table 2; co-ordinates with four places of decimals were used to calculate the bond lengths and angles given in Fig. 1. The low values found for the standard deviations are partly due to the small thermal motion observed at this temperature.

Table 3 shows the parameters of anisotropic thermal motion for the four heavy atoms, and the isotropic thermal motion for the hydrogen atoms. The $U_{ij}$ values, which give the magnitudes and orientation of the vibration ellipsoids with respect to the crystallographic axes, were used to calculate the principal axes of the vibration ellipsoids for each atom and their direction cosines with respect to the tetragonal axes (Table 4).[11] The direction of the maximum amplitude of vibration for the phosphorus atom almost coincides with the normal to the plane containing the phosphorus atom and the two adjacent nitrogen atoms. No simple correlation can be found relating a molecular axis with the ellipsoid of vibration for the nitrogen atom. The assumption was made that the molecule behaves as a rigid body in order that the anisotropic thermal parameters could be analysed into translational and oscillational




O P ○N ○C ●H

FIG. 3. A clinographic drawing of the structure. Molecules are shown whose centres are at **0**, $\frac{1}{2}$, $\frac{1}{8}$; **1**, $\frac{1}{2}$, $\frac{1}{8}$; **1**, $\frac{3}{4}$, $\frac{7}{8}$ (drawn with solid lines), and $\frac{1}{2}$, $\frac{1}{2}$, $\frac{3}{8}$; $\frac{1}{2}$, $\frac{1}{2}$, $-\frac{5}{8}$; $\frac{1}{2}$, $\frac{3}{4}$ $\frac{3}{8}$ (drawn with open bonds and dotted circles). Chain lines show the short H···H distances between interlocking methyl groups.

motion.[12] The results are given in Table 5, which also includes the corrections to the co-ordinates due to the rotational oscillations. The effects of these corrections [13] on the bond lengths and angles are very small (0·003 Å and less than 0·1°), because the intensity data were recorded at 140° K; they are not exact since the agreement between the observed and the calculated values of $U_{ij}$ indicate some internal vibrations. Since the corrections increase the uncertainty of the molecular dimensions they have been added to the standard deviations; the sum is shown in Fig. 1.

*Description of the Structure.*—The structure is composed of discrete molecules of $[PN(CH_3)_2]_4$, forming puckered eight-membered rings whose mean planes are parallel to the *ab* plane and related to each other by glide planes (Figs. 2 and 3). The ring consists of alternate phosphorus and nitrogen atoms related by $\bar{4}$ symmetry. The departure of the ring from planarity may be assessed by the difference in *z* co-ordinates of adjacent phosphorus (0·42 Å) and nitrogen atoms (1·08 Å).

[11] Cruickshank, *Acta Cryst.*, 1956, **9**, 747.
[12] Cruickshank, *Acta Cryst.*, 1956, **9**, 754.
[13] Cruickshank, *Acta Cryst.*, 1956, **9**, 757.

The molecular dimensions are shown in Fig. 1. The difference of $0{\cdot}009_6$ Å between the two P–N bond lengths ($1{\cdot}591_1$ and $1{\cdot}600_7$ Å) is not significant; [14]

$\sigma^2(\Delta 1) =$
$\sigma^2(P) + \sigma^2(N) - \sigma^2(P)\cos\angle NPN - \sigma^2(N)\cos\angle PNP$ in the direction P–N +
$\sigma^2(P) + \sigma^2(N) - \sigma^2(P)\cos\angle NPN - \sigma^2(N)\cos\angle PNP$ in the direction P′–N =
0·0049 Å

The P–C bond lengths ($1{\cdot}808_2$ and $1{\cdot}801_3$ Å) are not significantly different; $\sigma(\Delta 1) = 0{\cdot}0055$ Å.

Although the bisectors of the angles NPN′ and $C_1PC_2$ are almost collinear, the dihedral angle between the plane containing NPN′ and $C_1PC_2$ is 94° 46′.

Intermolecular distances are found to be greater than the sum of the van der Waals radii of the methyl groups (4·0 Å) with the exception of $C_1xyz \ldots C_2(\frac{1}{4} + y, \frac{1}{4} - x, -\frac{3}{4} + z)$, which is 3·68 Å.

## Discussion

The molecular geometry is unlikely to be greatly affected by van der Waals forces between molecules. Even within the molecule, distances between carbon atoms belonging to different phosphorus atoms can be varied without change of the ring angles at phosphorus and nitrogen. The distance $C_1$–$C_2$′ (3·93 Å), although only slightly altered by twisting a model of the molecule, may be increased to a value greater than 4 Å. This distance would be less than 3·9 Å if the angle PNP were only 120°; presumably compensation could be achieved by a more puckered ring and greater $C_1PN'$ and $C_2PN$ angles. It is thought, therefore, that in such a flexible molecule the angles in the ring are not controlled by van der Waals forces within the molecule.

The two P–N bond lengths (1·591 and 1·601 Å) are equal within experimental error, and are appreciably shorter than the sum of the single covalent radii [15] (1·76 Å), the value found in sodium phosphoramidate [16] (Table 6). The average P–N bond length is close to that in the trimeric phosphonitrilic chloride (Wilson *et al.*[2]) and to that quoted by Bullen [3]

Table 6.

Bond lengths of P–N and P–C in other structures (Å).

| P–N | σ | | Ref. | P–C | σ | | Ref. |
|---|---|---|---|---|---|---|---|
| 1·76 | 0·02 | $NaH_2NPO_3$ | 16 | 1·837 | 0·007 | $[H_2BP(CH_2)_2]_3$ | *b* |
| 1·653 | 0·005 | $(NH_2)_3PBH_3$ | *a* | 1·82, 1·84 | 0·015 | $[(C_2H_5)_2PS]_2$ | *c* |
| 1·66, 1·69 | | $(PNCl_2)_4$ | 2*a* | 1·82, 1·88 | | $[C_2H_5(CH_3)PS]_2$ | *d* |
| 1·57, 1·60, 1·61 | 0·017 | $(PNCl_2)_3$ | 2*b* | 1·813 | | $(CH_2)_2PO$ | *e* |
| 1·59 cyclic | | $\{PN[N(CH_3)_2]_2\}$ | 3 | 1·87 | 0·02 | $P(CH_3)_3$ | *f* |
| 1·75, 1·84 exocyclic | | | | 1·937 | 0·017 | $P(CF_3)_3$ | *g* |
| 1·49, 1·51, 1·52 | 0·02 | $(PNF_2)_4$ | 2*c* | 1·906 | 0·02 | $P(CF_3)_5$ | *h* |

*References*: (*a*) Nordman, *Acta Cryst.*, 1960, **13**, 535. (*b*) Hamilton, *Acta Cryst.*, 1955, **8**, 199. (*c*) Dutta and Wolfson, *Acta Cryst.*, 1961, **14**, 178. (*d*) Wheatley, *J.*, 1960, 523. (*e*) Wang, Forsvaretsforskningsinstitutt (Norway) Intern. Rapport IR–K–225 (1960). (*f*) Springall and Brockway, *J. Amer. Chem. Soc.*, 1938, **60**, 996. (*g*) Bowen, *Trans. Faraday Soc.*, 1954, **50**, 463. (*h*) Spencer and Lipscomb, *Acta Cryst.*, 1961, **14**, 250.

in his preliminary report on the structure of octakisdimethylamidotetraphosphonitrile. The length indicates partial double-bond character, as expected theoretically,[17] though the amount is presumably less than in the tetrameric fluoride (McGeachin *et al.*[2]), which has a shorter P–N bond. The P–C bond is a little shorter than the sum of the covalent radii [15] and is close to those reported for other organic compounds of quinquevalent phosphorus (Table 7).

The angle at the nitrogen atom in the present structure (132°) is greater than the 120° expected on the simplest basis, though the difference is less than for the fluoride. Such

[14] Cruickshank and Robertson, *Acta Cryst.*, 1953, **6**, 698.
[15] Pauling, " Nature of the Chemical Bond," Cornell University Press, 3rd edn., pp. 224, 229.
[16] Hobbs, Corbridge, and Raistrick, *Acta Cryst.*, 1953, **6**, 621; Cruickshank, unpublished work.
[17] Craig and Paddock, *Nature*, 1958, **181**, 1052; Craig, *J.*, 1959, 997; Dewar, Lucken, and Whitehead, *J.*, 1960, 2423.

an effect is common where chains and rings are formed from alternate first- and second-row elements, notably in octamethylcyclotetrasiloxane [18] (Si–O–Si = 143°), in octamethylcyclotetrasilazane [19] (Si–N–Si = 123°), and in ammonium [20] and sodium tetrametaphosphate [21] (P–O–P = 131° and 133°). The ring angle at phosphorus is almost the same in the octamethylcyclotetraphosphonitrile as in other tetrameric phosphonitriles. The exocyclic C–P–C angle is 104°; it is greater than the F–P–F angle in the fluoride (100°) because of the lower electronegativity of the methyl group.[22]

There is no indication of hydrogen bonding in the structure; all intermolecular C–N distances are greater than 3·59 Å, the sum of the van der Waals radii for the methyl group and nitrogen atom being 3·50 Å. However, a P–C bond of one molecule is directed towards a carbon atom on another to give the distance 3·68 Å; as a result two hydrogen atoms of $C_2(\frac{1}{4}+y, \frac{1}{4}-x, -\frac{3}{4}+z)$ fall in the spaces between the three hydrogen atoms on $C_1(x,y,z)$. Such interlocking of methyl groups has also been observed for sodium hydrogen diacetate,[23] and, aided by the high molecular symmetry, may account in part for the high melting point of the phosphonitrile.

It is a pleasure to thank Dr. M. R. Truter for her valuable advice and Dr. D. W. J. Cruickshank and Mr. N. L. Paddock for helpful discussion. I am grateful to the Directors and staff of the Computing Laboratory for carrying out the computations, to Albright and Wilson (Mfg.) Ltd. for financial support and to the Imperial Chemical Industries Limited for the loan of some of the equipment.

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[Seconded from Albright & Wilson (Mfg.) Ltd.] [*Received, July 11th*, 1961.]

[18] Steinfink, Post, and Fankuchen, *Acta Cryst.*, 1955, **8**, 420.
[19] Yokoi and Yamasaki, *J. Amer. Chem. Soc.*, 1953, **75**, 4139.
[20] Romers, Ketelaar, and MacGillavry, *Acta Cryst.*, 1951, **4**, 114; Cruickshank, unpublished work.
[21] Ondik, Block, and MacGillavry, *Acta Cryst.*, 1961, **14**, 555.
[22] Linnett and Mellish, *Trans. Faraday Soc.*, 1954, **50**, 657.
[23] Speakman and Mills, *J.*, 1961, 1164.

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## 1076. *Kinetics and Mechanism of Substitution at the Central Carbon Atom of Tri-*p*-nitrophenylmethyl Chloride in Glacial and Aqueous Acetic Acid.*

By Saul Patai and Jacob Zabicky.

Tri-*p*-nitrophenylmethyl chloride did not react with pure acetic acid; but in this solvent the chloride undergoes exchange with the anion of salts such as mercuric chloride or acetate, lithium chloride, and silver acetate, and in the presence of a strong acid it was solvolysed. In aqueous acetic acid the chloride was solvolysed giving the corresponding alcohol. In the presence of an added salt in acetic acid the rate-determining step of a proposed mechanism involves the formation of an ionised complex of tri-*p*-nitrophenylmethyl chloride and the metallic salt followed by a fast collapse of the complex into the triarylmethyl derivative of one of the anions involved in the complex. The mechanism is essentially the same in the solvolyses studied. No chlorine of zero or positive valency was liberated during these reactions or in the presence of *N*-chlorosuccinimide or t-butyl hypochlorite in glacial or aqueous acetic acid.

Solvolysis of triphenylmethyl chloride and replacement of its chlorine in other reactions have been the subject of extensive investigations and of controversial theories.[1,2] In

[1] Hughes, Ingold, Mok, Patai, and Pocker, *J.*, 1957, 1206—1279, and references quoted there.
[2] Swain, *J. Amer. Chem. Soc.*, 1948, **70**, 1119; Swain and Kreevoy, *ibid.*, 1955, **77**, 1122; Swain and MacLachlan, *ibid.*, 1960, **82**, 6095.

general it has been shown that the reaction is an $S_N$ process [1] and relatively fast. It has also been found [3] that in nitromethane, chlorobenzene, benzene, acetic acid, etc., the ion pair $Ph_3C^+Cl^-$ is obtained in the presence of electrophilic catalysts such as mercuric chloride. Most of the mechanisms suggested for replacements in the triphenylmethyl halide series [1,2,4] rule out the possibility of a normal $S_N2$ process. The reluctance of 1-bromotrypticene to undergo an $S_N$ reaction [5] indicates the improbability of an $S_N2$ process for triphenylmethyl halides, without inversion of configuration.

It was the aim of the present work to study the behaviour of a triarylmethyl halide of such an electronic structure that the ionisation of the carbon–halogen bond would not be facilitated, thus making an $S_N1$ mechanism improbable.

In tri-*p*-nitrophenylmethyl chloride, owing to the strongly electron-attracting substituents, the C–Cl bond will not undergo easy heterolysis into carbonium and chloride ions. Tri-*p*-nitrophenylmethyl bromide tends to undergo homolysis, *e.g.*, in basic media or in the presence of peroxides; [6] nevertheless it was hoped that the chloride would tend more towards heterolysis.

Although tri-*p*-nitrophenylmethylsodium in ether behaves as a strongly dissociated salt,[7] radical reactions such as oxidations were also observed.[6] Attempts to combine the postulated tri-*p*-nitrophenylmethyl anion with a carbonium ion such as the tri-*p*-methoxyphenylmethyl ion in order to produce a substituted hexaphenylethane with a carbon–carbon ion pair failed.[8]

## Results

Kinetic runs for the solvolysis and other exchange reactions of tri-*p*-nitrophenylmethyl chloride ($Ar_3CCl$) in glacial acetic acid or in water-containing acetic acid are summarised in Tables 1 and 2.

The kinetic runs were followed by measuring either the radioactivity of the chloride ions liberated from the organic chloride labelled with $^{36}Cl$ (method *a*), or by measuring the decrease in radioactivity of the labelled chloride and its derivatives obtained during the reaction (method *b*). The reproducibility of the results was good (compare runs 10—13, 14—15, 17—19, 29—31, 32—33, 34—36). Results in Table 1 conform well to first-order kinetics. Details of a typical kinetic run are given in Table 3.

Table 1 shows that no reaction * took place in acetic acid (runs 1, 2) or in this solvent in the presence of considerable concentrations of t-butyl hypochlorite, *N*-chlorosuccinimide, or lithium nitrate (runs 3—7). On the other hand, reaction took place in the presence of lithium chloride and of sulphuric acid (runs 8, 9).

The presence of water enhanced the reaction rate (compare runs 1,10, 29). In water-containing solutions the addition of a strong acid accelerated the reaction (runs 13, 24—28, 30, 32—33), although there was no acceleration for sulphuric acid concentrations higher than 0·07M and up to 0·18M. Added lithium chloride had an accelerating effect (runs 17—19). The results with added t-butyl hypochlorite in water-containing solutions showed an apparent slight slowing down in runs 20, 21, and an apparent slight acceleration in runs 22, 23. We believe that these small changes are caused solely by experimental errors when working with the volatile t-butyl hypochlorite. The Arrhenius activation energy of the solvolysis was calculated from runs 11, 14—16 as 20 kcal. $mole^{-1}$.

* Unless otherwise stated the term " reaction " implies any change in the $^{36}Cl$-labelled tri-*p*-nitrophenylmethyl chloride that enhances the radioactivity in the filtrate according to method *a*, or decreases the radioactivity in the precipitate according to method *b*.

[3] Evans, Price, and Thomas, *Trans. Faraday Soc.*, 1954, **50**, 568; 1955, **51**, 481; 1956, **52**, 332; *J.*, 1957, 4644; Bayles, Evans, and Jones, *J.*, 1955, 206, 3104; 1957, 1020; Cotter and Evans, *J.*, 1959, 2988.

[4] Read and Taylor, *J.*, 1939, 478.

[5] Bartlett and Lewis, *J. Amer. Chem. Soc.*, 1950, **72**, 1005.

[6] Leffler, *J. Amer. Chem. Soc.*, 1953, **75**, 3598.

[7] Ziegler and Wolschitt, *Annalen*, 1930, **479**, 123.

[8] Leffler, " The Reactive Intermediates of Organic Chemistry," Interscience Publ. Inc., New York, 1956, p. 17.

Table 2 records the second-order reaction coefficient found for the reaction with lithium chloride in acetic acid. It was impossible to carry out runs with initial concentrations differing much from those used, owing to the low solubility of tri-*p*-nitrophenylmethyl chloride in acetic

TABLE 1.

First-order rate coefficients [a] for the solvolysis of tri-*p*-nitrophenylmethyl chloride in acetic acid at 30°.

| Run | $10^3[Ar_3CCl]_0$ (mole l.$^{-1}$) | Concn. of added substance (mole l.$^{-1}$) | $10^3k$ (min.$^{-1}$) |
|---|---|---|---|
| | In glacial AcOH | | |
| 1 [b] | 2·36 | — | 0·00 |
| 2 [c] | 5·92 | — | 0·00 |
| 3 [d] | 3·02 | 0·20 $Bu^tOCl$ | 0·00 |
| 4 [e, e] | 3·43 | 1·48 ,, | 0·00 |
| 5 [f] | 2·22 | 1·48 ,, | 0·00 |
| 6 [g] | 2·37 | 0·44 NCS [h] | 0·00 |
| 7 [e] | 1·16 | 0·177 $LiNO_3$ | 0·00 |
| 8 | 2·14 | 0·426 LiCl | 0·10 |
| 9 | 4·65 | 0·362 $H_2SO_4$ | 0·20 |
| | Acid containing 20% v/v of water | | |
| 10 | 1·35 | — | 0·46 |
| 11 | 1·52 | — | 0·44 |
| 12 | 1·98 | — | 0·44 |
| 13 | 4·06 | — | 0·43 |
| 14, 15 [i] | 2·37 | — | 1·52, 1·63 |
| 16 [j] | 2·37 | — | 4·40 |
| 17 | 1·53 | 0·426 LiCl | 1·30 |
| 18 | 1·82 | 0·426 ,, | 1·20 |
| 19 | 1·85 | 0·426 ,, | 1·18 |
| 20 | 4·57 | 0·20 $Bu^tOCl$ | 0·34 |
| 21 | 6·04 | 0·20 ,, | 0·40 |
| 22 | 4·02 | 0·74 ,, | 0·47 |
| 23 [e] | 3·86 | 0·74 ,, | 0·48 |
| 24 | 2·88 | 0·0362 $H_2SO_4$ | 0·88 |
| 25 | 2·88 | 0·0724 ,, | 1·74 |
| 26 | 2·88 | 0·1086 ,, | 1·74 |
| 27 | 2·88 | 0·1448 ,, | 1·74 |
| 28 | 2·88 | 0·1810 ,, | 1·74 |
| | Acid containing 30% v/v of water | | |
| 29 | 9·26 | — | 2·01 |
| 30 | 5·07 | — | 2·39 |
| 31 | 3·85 | — | 2·20 |
| 32 | 3·77 | 0·1448 $H_2SO_4$ | 3·24 |
| 33 | 4·03 | 0·1448 ,, | 3·42 |

[a] Sampling method *b* (see text) was used in runs 4, 22, and 23, in all others method *a*. [b] Run followed for 8 days. [c] Run followed for 3 weeks. [d] Run followed for 2·5 hr. [e] Run followed for 3 hr. [f] Run followed for 4 days. [g] Run followed for 6 days [h] *N*-Chlorosuccinimide. [i] At 40·3°. [j] At 50·3°.

TABLE 2.

Second-order [a] rate coefficients [b] for the reaction of tri-*p*-nitrophenylmethyl chloride and lithium chloride in glacial acetic acid at 40·3°.

| Run | $10^3[Ar_3CCl]_0$ (mole l.$^{-1}$) | $10^3[LiCl]_0$ (mole l.$^{-1}$) | $10^3k$ (l. mole$^{-1}$ hr.$^{-1}$) |
|---|---|---|---|
| 34 | 2·88 | 76·8 | 1·40 |
| 35 | 3·84 | 76·8 | 1·39 |
| 36 | 3·84 | 127·9 | 1·27 |

[a] First-order in each of $Ar_3CCl$ and LiCl. [b] Determined by sampling method *a* (see text).

TABLE 3.

Kinetic details of run 13 (Table 1).

| Sample | 1 | 2 | 3 | 4 | 5 | 6 |
|---|---|---|---|---|---|---|
| Time (min.) | 2 | 10 | 26 | 43 | 63 | 87 |
| Reaction (%) | 1·2 | 3·1 | 10·4 | 16·5 | 24·5 | 30·6 |
| $10^3k$ (min.$^{-1}$) | 0·5 | 0·3 | 0·42 | 0·42 | 0·44 | 0·43 |

acid on the one hand, and to very low reaction rates obtained with much lower initial concentrations of lithium chloride on the other.

Other qualitative experiments (see Experimental) gave the following results: Product analysis showed that in water-containing acetic acid the chloride was hydrolysed to tri-*p*-nitrophenylmethanol. It reacted slowly with silver acetate in acetic acid (giving silver chloride) and with mercuric chloride (undergoing chlorine exchange); when mercuric acetate was used instead of the chloride, chloride ions were liberated into the solution and the water-insoluble

product was the organic acetate. The organic chloride underwent chlorine exchange with lithium chloride. No carbonium ions or ion pairs were formed in spectrophotometrically measurable concentrations when the chloride was dissolved in acetic acid containing various concentrations of mercuric chloride. In aqueous acetone it reacted with sodium hydroxide, liberating chloride ions; in this reaction colour changes occurred that are probably due to a homolytic process similar to those described by Leffler.[6] No reaction was detected in dry acetone or for a suspension in aqueous sodium hydroxide. No liberation of chlorine in a form capable of oxidizing iodide ions was detected during the solvolysis in aqueous acetic acid.

## Discussion

The following mechanism is proposed for the exchange reactions of tri-*p*-nitrophenylmethyl chloride in acetic acid:

$$RCl + MX \underset{\text{Fast}}{\overset{\text{Slow}}{\rightleftharpoons}} R^+(ClMX)^- \underset{\text{Slow}}{\overset{\text{Fast}}{\rightleftharpoons}} RX + MCl$$

(1) (2)

Step (1) represents the slow reaction with a metal salt [MX = $HgCl_2$, $Hg(OAc)_2$, LiCl, AgOAc], involving either ionisation of the organic chloride aided by electrophylic catalysis or possibly the formation of a quadruple ion composed of the organic chloride and the metal salt (see ref. 1, pp. 1265 *et seq.*). In either case the intermediate may collapse fast into the covalent form either by reversing step (1) or metathetically by step (2).

The following results support this mechanism: No reaction takes place by solvolysis in pure acetic acid, while in the same medium, in the presence of mercuric chloride (both the organic and the inorganic chloride in low concentrations), 70% exchange has been measured. In these conditions the solvolysis, if any, by acetic acid was less than 4%, *i.e.*, within the experimental error. We believe, therefore, that formation of ionised intermediates (ion pairs or quadrupoles) takes place, aided by the mercuric chloride, and that collapse of these leads to chlorine exchange. In other words, an ion pair of the form $R^+Cl^-$ which is at least partially solvated by mercuric chloride gives returns to the organic halide molecule in which the chlorine may originate from the mercuric chloride, while practically no collapse to the corresponding acetate takes place notwithstanding the large excess of acetic acid in the vicinity. As mercuric acetate strongly catalyses the exchange of chlorine for acetate, it seems that the function of the metal atom is to aid distention of the C–Cl bond to a point where the collapse to the original molecule is not dominant but new C–Cl (in the case of $HgCl_2$) or C–OAc [in case of $Hg(OAc)_2$] bonds can be formed. The anions attached to the mercury atom will be in a preferential position for a nucleophilic attack on the central carbon atom. The second-order kinetics of the exchange with lithium chloride that was observed even with a large excess of the salt reinforce the argument for a slow rate of step (1). The failure to detect a measurable concentration of an ionised intermediate tends to show that its disappearance is faster than its formation.

The acceleration caused by added strong acid (run 9) can be explained similarly:

$$RCl + H^+ \underset{\text{Fast}}{\overset{\text{Slow}}{\rightleftharpoons}} R^{\delta+} \cdots Cl^{\delta-} \cdots H^{\delta+} \xrightarrow[\text{Fast}]{\text{AcOH (Solvent)}} ROAc + HCl + H^+$$

It is believed that the mechanism of solvolysis in aqueous acetic acid is essentially the same as that of the salt-catalysed exchange. On the basis of our experiments, we are unable to decide whether the alcohol is formed directly, owing to the preferential solvation by water, or through the acetate with subsequent hydrolysis, or by both routes simultaneously:

$$RCl + HOH \underset{\text{Fast}}{\overset{\text{Slow}}{\rightleftharpoons}} R^+(ClH_2O)^- \underset{\text{Fast}}{\overset{\text{Slow}}{\rightleftharpoons}} ROH + HCl$$

The rate acceleration caused by larger amounts of water may be due to the enhancement

of the dielectric constant of the solvent, thus aiding the separation of charges in the ionic intermediate. The observed acceleration by added lithium chloride may be caused by a positive salt effect as well as by the effect of the salt as an added nucleophilic reagent.

The proposed mechanism of reaction involves implications on the stereochemistry of the chlorine exchange: the reaction has to proceed without inversion of configuration, as the leaving and the entering group are placed on the same side of the molecule in respect to the phenyl groups.

Electrophilic catalysis by protons is probably the cause of the rate enhancement by added sulphuric acid in aqueous acetic acid. The sulphuric acid concentration is low enough not to change the medium essentially. A limit in the acid catalysis is reached with $2{\cdot}88 \times 10^{-3}$M-tri-*p*-nitrophenylmethyl chloride in 1 : 4 water–acetic acid when the sulphuric acid concentration is about 0·07M. The 25-fold concentration of sulphuric acid (as compared with that of the organic chloride) seems to supply sufficient protons to the solvation shell in the immediate vicinity of the reacting groups for higher acid concentrations to have no additional effect.

It has been postulated [6] that triaryl halides with electron-attracting substituents may ionise, $Ar_3CX \rightleftharpoons Ar_3C^- + X^+$. Our chloride does not react in presence of t-butyl hypochlorite as a possible source of positive or free chlorine,[9] in acetic acid or in 1 : 4 water–acetic acid, or in presence of *N*-chlorosuccinimide in acetic acid.[10] Thus our chloride has no tendency to undergo electrophilic or radical replacement at its central carbon atom in these conditions. Lack of reaction of potassium iodide with the mother liquors of the reaction also showed that our chloride does not liberate either free or positive chlorine.

## Experimental

*Tri-*p*-nitrophenylmethyl Chloride.*—The synthesis was carried out in the apparatus shown in the Figure, under a hood. Tri-*p*-nitrophenylmethane [11] (4 g.) in a 200 ml. flat-bottomed flask (1) provided with a magnetic stirrer was dissolved in the minimal amount of dry pyridine by stirring and slight heating (infrared lamp). A stream of dry, oxygen-free nitrogen was passed continuously through tap (2), with all other taps closed. After cooling of flask (1), sodium (2 g.), dissolved in the minimum amount of absolute ethanol, was added through the funnel (3) with constant stirring during 2 min., giving a deep-blue suspension of tri-*p*-nitrophenylmethylsodium. Ether (100 ml.) was added through funnel (3) and the suspension stirred for 1 min. and left to settle for 10 min. About half of the ether layer was sucked out carefully through tap (4) into a trap connected to a vacuum, care being taken that no solid was carried over. The washing with ether was repeated until the ether became colourless or only very faintly blue after the sedimentation of the organosodium compound. The precipitate was a glistening copper-coloured solid. Part of the ether was sucked out, tap (4) closed, and the residue evaporated by increasing the nitrogen flow and heating the stirred suspension (infrared lamp) until the precipitate was almost dry. Drying was completed with the nitrogen stream alone. (This part of the procedure is a variation of the method given in ref. 12.) Dry carbon tetrachloride (120 ml.) was added through the funnel (3) and the mixture was vigorously stirred. With taps (5) and (6) open a stream of nitrogen was passed through tap (6) in order to expel all the air; tap (5) was closed, tap (7) opened, and a slow current of chlorine passed through tap (6) into the suspension. The nitrogen flow was stopped and a trap for chlorine (potassium iodide solution) attached to tube (8). The chlorine flow was maintained until the dark solid had all become yellow, then the mixture was left overnight. The solid was filtered off on sintered glass and washed with carbon tetrachloride. Recrystallisations from benzene give a light yellow powder, m. p. 196—198° (Found: C, 55·6; H, 3·0; Cl, 8·35; N, 9·85. Calc. for $C_{19}H_{12}ClN_3O_6$: C, 55·2; H, 2·9; Cl, 8·6; N, 10·2%), and a second fraction of efflorescent

[9] Winkler and Hearne, *J. Org. Chem.*, 1960, **25**, 1835; Walling and Jacknow, *J. Amer. Chem. Soc.*, 1960, **82**, 6108, 6113.
[10] Robertson and Waters, *J.*, 1947, 492; Cosgrove and Waters, *J.*, 1949, 907; Hebbelynck and Martin, *Bull. Soc. chim. belges*, 1950, **59**, 193; 1951, **60**, 54.
[11] Shoesmith, Sosson, and Hetherington, *J.*, 1927, 2221.
[12] Ziegler and Boye, *Annalen*, 1927, **458**, 248.

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orange crystals that melt at a low temperature, resolidify, and melt again at 195°; the latter form is believed to contain benzene of crystallisation, and recrystallisation from acetone gave yellow crystals, m. p. 208°, whose analysis and infrared spectrum coincided with those of the powder described above. The yield was 20—30%. A previous attempt to synthesise this compound was reported by Gomberg.[13]

To obtain the $^{36}$Cl-labelled compound a modification of the method described by Brown *et al.*[14] was used: a suspension of " AnalaR " potassium persulphate (15 g.) in water (50 ml.) was placed in a flask (9) mounted in a water bath, taps (5), (10), and (11) were opened, and a vigorous nitrogen stream bubbled into flask (9) through tap (10). The water bath was heated to 70° and labelled 0·5N-hydrochloric acid (5 ml.) added through funnel (12). Tap (7) was opened and taps (2) and (5) were closed. Oxidation of the hydrochloric acid required 1—2 hr. Chlorination of the suspension in flask (1) was completed by stopping the nitrogen stream through tap (10), closing tap (11), and passing through tap (6) a slow current of chlorine as described above. The labelled compound was purified as described above.

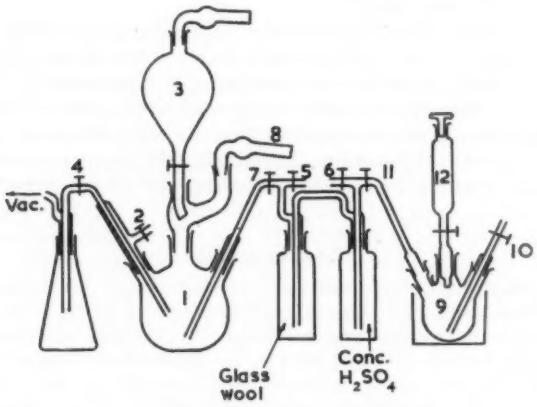


FIG. 1.

*Other Materials.*—Sulphuric and glacial acetic acid were analytical reagents. Distilled water was used. Lithium chloride (" AnalaR ") was powdered and then dried in an oven at 110° to constant weight. *N*-Chlorosuccinimide, silver acetate, mercuric chloride (all from B.D.H.), and mercuric acetate (Baker's " Analysed ") were used without purification. t-Butyl hypochlorite was prepared and purified as described by Teeter and Bell; [15] stock solutions in acetic acid were stable in tightly stoppered, all-glass bottles in the dark; the hypochlorite content was determined before use by iodometric titration.

*Kinetic Runs.*—Solutions of the reagents were kept in a water bath at the required temperature, then mixed, made up to volume, and placed in the water bath. Samples were processed by one of the following methods:

(*a*) The reaction mixture (3 ml.) was placed in a 10 ml. measuring flask, filled with water to the mark, shaken, and placed for several minutes in an ice–salt bath. A suspension of " Celite " filter aid (Johns-Manville) in water was filtered through a coarse sintered-glass funnel, to provide a layer of about 2 mm. The reaction mixture was filtered and the radioactivity of the filtrate was measured.

(*b*) The reaction mixture (5 ml.), in a 25 ml. measuring flask, was treated and filtered as in method *a* and the flask washed repeatedly with small amounts of cold water that were poured on the precipitate. The precipitate and " Celite " were transferred to the measuring flask, the funnel washed repeatedly with acetone into the flask, and the latter filled to the mark with

[13] Gomberg, *Ber.*, 1904, **37**, 1626.
[14] Brown, Gillies, and Stevens, *Canad. J. Chem.*, 1953, **31**, 768.
[15] Teeter and Bell, *Org. Synth.*, 1952, **32**, 20.

the same solvent. The suspension was shaken and left to settle and 10 ml. of the overlying solution were taken for measurement.

Radioactivity measurements were carried out in a Geiger–Müller tube attached to a scaler (Ekco Electronics Ltd., type N529A). The background radiation and a suitable sample representing 0 or 100% reaction were measured each day.

*Various.*—Infrared spectra were determined in an " Infracord " Perkin-Elmer spectrophotometer. Ultraviolet spectra were determined in a Beckman DU spectrophotometer. M. p.s were determined on a Kofler heating stage.

The following experiments were also carried out (" organic chloride " refers to tri-*p*-nitrophenylmethyl chloride):

(I) The organic chloride (100 mg.) was refluxed for 5 hr. in acetic acid (120 ml.) containing 20% v/v of water; the product was precipitated with water, filtered, and recrystallised from acetic acid–ligroin; it had m. p. 186° and was identified as tri-*p*-nitrophenylmethanol by a mixed m. p. [lit., 188—189°, 189°, 193° (corr.); see refs. 16, 13, and 17] and by its infrared spectrum.

(II) $2{\cdot}36 \times 10^{-2}$M-Organic chloride (45 ml.) in acetic acid, mixed with a saturated solution (5 ml.) of silver acetate in the same solvent, was kept at 30°. After a few minutes the solution became turbid. After 2 days the precipitate was isolated and identified as silver chloride.

(III) $6{\cdot}21 \times 10^{-2}$M-Organic chloride in dry acetone gave no chloride or other water-soluble ion containing chlorine in 3 hr. at 30°.

(IV) The organic chloride (15 mg.) was refluxed for 1 hr. in suspension in 5% aqueous sodium hydroxide (100 ml.). No chloride ions were detected in the filtered solution by Volhard's method.

(V) $5{\cdot}22 \times 10^{-2}$M-Organic chloride in acetone containing 15% v/v of water and 1% w/v of sodium hydroxide gave after 1 hr. at 30° almost complete liberation of chloride and other water-soluble ions containing chlorine. The solution changed its colour in the first minutes of the reaction from colourless to green, then to dark blue; after 2 days' exposure to air the colour changed to red and finally to dark yellow.

(VI) The ultraviolet spectrum of the organic chloride was determined in acetic acid ($\lambda_{max.}$ 268 mμ, ε $3{\cdot}1 \times 10^4$). A $5 \times 10^{-5}$M-solution in a saturated solution of mercuric chloride in acetic acid was kept at 30° and the spectrum was determined after 2 hr. and after 2 days; in each case the spectrum coincided, within the limits of experimental error, with that of the organic chloride alone in acetic acid in the range 250—320 mμ. Similar results were obtained with more dilute solutions of mercuric chloride.

(VII) Various samples were taken by method *a* from runs 10, 11, 12, 13 (7, 12, 30, 41% reaction). When the filtrates were treated with aqueous potassium iodide solution, no iodine was liberated.

(VIII) An acetic acid solution $1{\cdot}92 \times 10^{-3}$M in labelled organic chloride and $2{\cdot}73 \times 10^{-3}$M in mercuric chloride was kept at 40·3°. Approximately 70% of the radioactive chlorine was liberated. The mixture with cold water gave a precipitate which melted at 195° and gave the correct chlorine analysis for the organic chloride (Found: Cl, 8·25%).

(IX) An acetic acid solution $3{\cdot}84 \times 10^{-3}$M in organic chloride and $2{\cdot}07 \times 10^{-3}$M in mercuric acetate was kept for 3 days at 40·3°. Tri-*p*-nitrophenylmethyl acetate, precipitated on addition of cold water, was filtered off and washed (m. p. 95—98°) (Found: Ac, 12·0. Calc. for $C_{21}H_{15}N_3O_8$: 1Ac, 11·9%).

(X) An acetic acid solution $3{\cdot}58 \times 10^{-3}$M in labelled organic chloride and 0·282M in lithium chloride was kept at 40·3°; after 7 days about 50% of the radioactive chlorine had been liberated. The solid precipitated on addition of cold water was filtered off and washed; it had m. p. 160° (Found: Cl, 7·3%); it was probably a mixture of about 85 mole-% of the organic chloride and 15 mole-% of the acetate.

Department of Organic Chemistry, The Hebrew University, Jerusalem, Israel. [*Received, July 4th*, 1961.]

[16] Fischer and Fischer, *Annalen*, 1878, **194**, 242.
[17] Montagne, *Rec. Trav. chim.*, 1905, **24**, 127.

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## 1077. *The Rôle of* 3d-*Orbitals in π-Bonds between* (a) *Silicon, Phosphorus, Sulphur, or Chlorine and* (b) *Oxygen or Nitrogen.*

By D. W. J. Cruickshank.

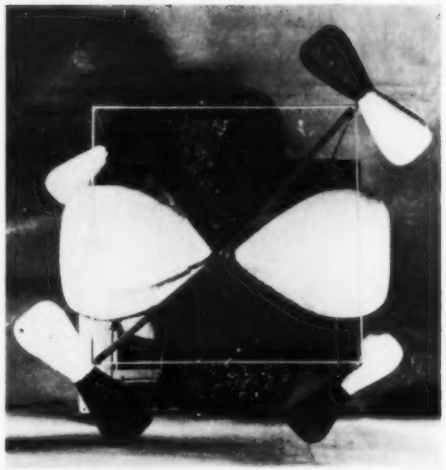
In the $XO_4^{n-}$ tetrahedral ions (X = Si, P, S, or Cl) two strong π-bonding molecular orbitals are formed with the $3d_{x^2-y^2}$ and $3d_{z^2}$ orbitals of X and the appropriate $2p\pi$ and $2p\pi'$-orbitals of oxygen. This explains the contraction of the S–O bond, say, from the presumed 1·69 Å for a single bond to 1·49 Å in $SO_4^{2-}$. In ethyl sulphate the ester-oxygen still has a share in one π-orbital, which explains its intermediate S–O value of 1·60 Å. The ability of doubly linked oxygen and triply linked nitrogen to share in the π-bond systems generated by tetrahedrally co-ordinated X is widespread. An interpretation is given of the structures of $[S_2O_7]^{2-}$, $[NH(SO_3)_2]^{2-}$, $[CH(SO_3)_2]^{2-}$, $SO_3NH_3$, $[SO_3NH_2]^-$, $SO_2(NH_2)_2$, and $(SO_3)_\infty$ in terms of the π-bond systems. Structures with tetrahedral phosphorus and silicon are similarly discussed, with special attention to those with XOX angles of 140—180°. In ions containing hydroxyl groups, the bonds are intermediate in length between those for the ion without the proton and for the ion with R in place of H, apparently owing to hydrogen-bond formation. The use of $d_{x^2-y^2}$ and $d_{z^2}$ orbitals for π-bonding is of potential importance whenever X is tetrahedrally co-ordinated and must be considered in, say, $RSO_3^-$, $R_2SO_2$, and $RSO_2^-$. X–F bonds and the π-bond systems in $[PNF_2]_4$ and $[PN(CH_3)_2]_4$, etc., are also discussed.

The single system of π-orbitals in planar aromatic molecules is well known. This paper presents evidence for a double system of π-orbitals in sulphates, phosphates, silicates, etc., the orbitals extending throughout the molecules. The discussion is restricted to molecules in which silicon, phosphorus, sulphur, or chlorine atoms are tetrahedrally co-ordinated. The bonding in the $XO_4^{n-}$ ions is considered first, and the description is extended successively to molecules in which the oxygens are linked also to other atoms or to other tetrahedra, to molecules in which nitrogen and other atoms are ligands of X, and to molecules in which lone pairs of X occupy some of the tetrahedral positions. Thus, ions such as $[C_2H_5{\cdot}SO_4]^-$, $P_2O_7^{6-}$, $SO{\cdot}NH_3^+$, and $ClO_3^-$ are discussed, but not $SO_3$ or $SO_2$. The theme of the paper is thus summarised in its title. The π-orbital system is a double one in the sense that two *d*-orbitals of X, $d_{x^2-y^2}$ and $d_{z^2}$, are used simultaneously when X is tetrahedrally co-ordinated. The experimental evidences appealed to in this paper are the observed bond lengths in a large number of molecules, many of which have been recently determined or refined in this Department by *X*-ray crystallographic methods. The main features of the paper were reported [1] briefly at the Congress of the International Union of Crystallography at Cambridge in August, 1960.

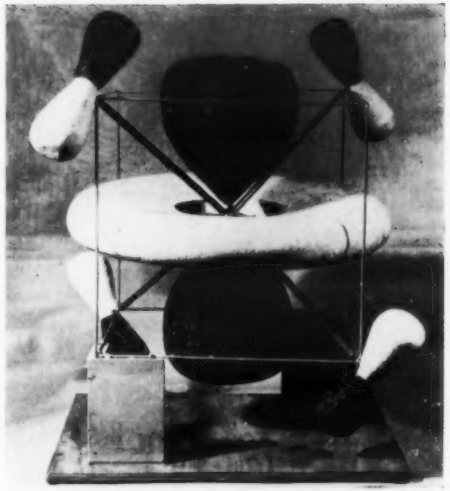
Estimated standard deviations (e.s.d.'s) for the observed bond lengths quoted in this paper are shown in the style " ±0·01 Å." Some of these e.s.d.'s are larger than those quoted by the original authors. Such increases have been made to cover more recently discovered types of systematic error, etc. The rotational-oscillation effect,[2] in particular, has often altered bond lengths by 0·005—0·01 Å or even 0·03 Å. In a few instances no e.s.d.'s were quoted by the original authors and estimates have been made subjectively by the present writer. Some attention should be paid to the e.s.d.'s quoted for the observed results, as the analyses range from those with e.s.d.'s of 0·004 Å in the X–O bonds to others with e.s.d.'s of 0·03 Å or so. The results for some relevant structures have had to be excluded because their precision, judged by modern standards, is too uncertain.

This investigation arose out of the results of the *X*-ray crystal-structure analysis of nitronium perchlorate [3] in which the Cl–O bond length in the discrete $ClO_4^-$ ion was

[1] Cruickshank, *Acta Cryst.*, 1960, **13**, 1033.
[2] Cruickshank, *Acta Cryst.*, 1956, **9**, 757; 1961, **14**, 896.
[3] Truter, Cruickshank, and Jeffrey, *Acta Cryst.*, 1960, **13**, 855.



(a) Overlap of $X(d_{x^2-y^2})$ with oxygen $2p\pi$ in $XO_4^{n-}$.



(b) Overlap of $X(d_{z^2})$ with oxygen $2p\pi'$.

[*To face p. 5487.*

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determined as 1·46 ± 0·01 Å.* This bond length is appreciably shorter than the 1·685 Å expected [7] for a single bond or the 1·70 ± 0·02 Å found [8] in $Cl_2O$. The double-bond character of the bonds in the isoelectronic $SiO_4^{4-}$, $PO_4^{3-}$, $SO_4^{2-}$, and $ClO_4^-$ tetrahedral ions has been often stressed previously, but we shall consider it again here in more detail. In Table 1 we compare the observed bond lengths, whose e.s.d.'s are about 0·01 Å, with the expected single-bond distances and we see that the shortenings increase from perhaps 0·13 Å in $SiO_4^{4-}$ to $0{\cdot}22_5$ Å in $ClO_4^-$. The symmetrical stretching force constants [9] are also greater than for typical single bonds, though the sequence of values P–O 9·05, S–O 9·07, and Cl–O 8·24 mdyne/Å does not indicate the Cl–O bond as the stiffest.

TABLE 1.

Bond lengths in $XO_4^{n-}$ ions Å.

| | Si–O | P–O | S–O | Cl–O |
|---|---|---|---|---|
| Single-bond value * | 1·76 | 1·71 | 1·69 | $1{\cdot}68_5$ |
| Observed | 1·63 † | 1·54 ‡ | 1·49 § | 1·46 |
| Contraction | 0·13 | 0·17 | 0·20 | $0{\cdot}22_5$ |

* Calculated by the Schomaker–Stevenson equation.[7] † Average derived from analyses of spurrite $Ca_5(SiO_4)_2CO_3$ (Smith, Karle, Hauptman, and Karle, *Acta Cryst.*, 1960, **13**, 454), grossularite $Ca_3Al_2(SiO_4)_3$ (Abrahams and Geller, *ibid.*, 1958, **11**, 437), and $\beta$-$Ca_2SiO_4$ (Midgeley, *ibid.*, 1952, **5**, 307; Cruickshank, unpublished work). ‡ Average from hydroxyapatite $Ca_{10}(PO_4)_6(OH)_2$ (Posner, Perloff, and Diorio, *Acta Cryst.*, 1958, **11**, 308), and $LiMnPO_4$ (Geller and Durand, *Acta Cryst.*, 1960, **13**, 325) with approximate rotational corrections considered. § From gypsum $CaSO_4,2H_2O$ (Atoji and Rundle, *J. Chem. Phys.*, 1958, **29**, 1306).

*Nature of the π-Bonding in the* $XO_4^{n-}$ *Ions.*—In the $XO_4^{n-}$ ions, after electrons have been allotted to the inner shells, to four tetrahedral $sp^3$ σ-bonds, and to four σ-lone pairs at the back of each oxygen atom, there remain 16 electrons needing eight molecular orbitals. These orbitals may be built from the available atomic orbitals, which are the $2p\pi$ and $2p\pi'$ on each oxygen (so that the oxygens alone could provide the eight orbitals) and the five 3*d*-orbitals of the central X atom. The combinations of the 3*d*- and oxygen 2*p*-orbitals are settled by group theory applied to the point group $T_d$ (see Eyring *et al.*[10] for notation and methods; note, however, that their character table for $T_d$ erroneously interchanges the characters for $T_1$ and $T_2$ representations). There prove to be two strongly π-bonding molecular orbitals in the representation $E$, three weakly π-bonding molecular orbitals in $T_2$, which are effectively lone-pair combinations, and three non-bonding combinations of oxygen orbitals in $T_1$, thus giving the eight desired orbitals.

One of the two strong π-bonding molecular orbitals uses the $d_{x^2-y^2}$ orbital. The excellent overlap of this with the oxygen combination $\frac{1}{2}(p_1 + p_2 + p_3 + p_4)$ is shown in Plate 1a. The other uses $d_{z^2}$ with $\frac{1}{2}(p_1' + p_2' + p_3' + p_4')$ and is shown in Plate 1b. Here $p_1$, $p_2$, $p_3$, $p_4$ are the $2p\pi$-orbitals perpendicular to the $z$-axis of the tetrahedron and $p_1'$, $p_2'$, $p_3'$, $p_4'$ are the corresponding $2p\pi'$-orbitals on the four oxygen atoms. The models illustrated in the Plates are only schematic. For each atom the black and the white lobes represent regions in which the atomic wave functions are positive and negative. The *d*-orbits should be thought of as much larger than the *p*-orbits, since they actually diffuse well into the region of the latter. Further, in the $d_{z^2}$ orbit the amplitude of the

* This value is slightly larger than those reported in some other recent analyses, but in one of them, the room-temperature form [4] of $H_3O^+ClO_4^-$ which M. R. Truter [5] has refined, a substantial rotational-oscillation correction [2] of 0·027 Å satisfactorily increases the Cl–O length to $1{\cdot}45_2^2$ ± 0·005 Å. A good analysis [6] of the ordered low-temperature form of $H_3O^+ClO_4^-$ gives a mean Cl–O length of 1·462 ± 0·004 Å.


[4] Lee and Carpenter, *J. Phys. Chem.*, 1959, **63**, 279.
[5] Truter, *Acta Cryst.*, 1961, **14**, 318.
[6] Nordman, *Acta Cryst.*, 1960, **13**, 1030; private communication.
[7] Schomaker and Stevenson, *J. Amer. Chem. Soc.*, 1941, **63**, 37.
[8] Dunitz and Hedberg, *J. Amer. Chem. Soc.*, 1950, **72**, 3108.
[9] Herzberg, "Molecular Spectra and Molecular Structure," Vol. II, Van Nostrand Co., Princeton, 1945.
[10] Eyring, Walter, and Kimball, "Quantum Chemistry," John Wiley, New York, 1944.


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wave function along the $\pm z$ axes is twice the amplitude at the equator for the same radius (which is why the conventional polar diagram shows only a small equatorial band). Since the maximum amplitude of $\psi$ occurs at the same radius for both the equatorial band and the axial lobes, the model had been made with band and lobes of similar maximum radius in order to bring out the geometrical suitability of the $d_{z^2}$-orbit for π-bonding.

As shown in the Plates, the nodes of each 3*d*-orbital pass through the oxygen positions, so that the positive and negative lobes of the *p*-orbitals lie nicely in the corresponding regions of the *d*-orbitals. The group overlap integrals for these two π-bonding molecular orbitals are identical and are $(8/3)^{\frac{1}{2}} = 1{\cdot}63$ times the maximum possible overlap of an X 3*d*-orbital with one 2*p*-orbital at the same internuclear distance. The absolute values of the overlap integrals are not easy to estimate. The arguments of Appendix I, based on self-consistent-field calculations for the first long row, suggest a value of 0·6 in the perchlorate ion. This Cl (3*d*) : O(combination) group overlap is about twice that of adjacent *p*π-orbits in benzene, so that it is not surprising that the Cl–O distance in the perchlorate ion is $0{\cdot}22_5$ Å shorter than a single bond.

The three orbitals in $T_2$ are

$$(1/2)^{\frac{1}{2}}\,(d_{xz} - d_{yz}) \text{ with } (3/8)^{\frac{1}{2}}(p_1 - p_2) + (1/8)^{\frac{1}{2}}(p_3' - p_4')$$

$$(1/2)^{\frac{1}{2}}\,(d_{xz} + d_{yz}) \text{ with } (3/8)^{\frac{1}{2}}(p_3 - p_4) + (1/8)^{\frac{1}{2}}(p_1' - p_2')$$

$$d_{xy} \qquad\qquad \text{with } (1/2)(-p_1' - p_2' + p_3' + p_4')$$

The overlaps of the X and oxygen combination orbitals of $T_2$ symmetry are not as good as those of $E$ symmetry; for example, with $d_{xy}$, while one lobe of each oxygen *p*-orbital dips into a lobe of $d_{xy}$, the other *p*-orbital lobe points away into a region where $d_{xy}$ is of low density and wrong sign. If $d_{xy}$, $d_{yz}$, and $d_{xz}$ had the same radial size as $d_{x^2-y^2}$, the three orbitals of $T_2$ would have overlap integrals $\sqrt{3}$ times lower than the orbitals of $E$. In fact these three *d*-orbitals will be more diffuse, partly because of repulsion by the σ-bonds and partly because the $T_2$ orbitals will be of higher energy than the $E$ orbitals; consequently the overlaps will be further reduced. Also these $T_2$ molecular orbitals are probably very heteropolar,[11] since they have the highest energy of any filled orbitals which could be heteropolar. We may therefore infer that the orbitals of the $T_2$ representation play a much smaller effective part in the π-bonding system of the $XO_4^{n-}$ ions and that they can be treated as three weakly π-bonding orbitals.

In a previous application of group theory to these tetrahedral ions Wolfsberg and Helmholtz [12] obtained rather more cumbersome forms of the molecular orbitals than those given above and showed that the group overlaps for the $E$ and $T_2$ orbitals differed by a factor of $\sqrt{3}$. Strictly speaking, only their numerical values showed this factor; owing to a misprint their two analytical expressions were identical. By an uncritical use of the Slater screening constants, they concluded that 3*d*-orbitals were not important in $ClO_4^-$ though they were in $MnO_4^-$.

In an important paper Jaffé,[13] by working from electronegativities and the consequent charge shifts in the X–O σ-bonds, derived a value of 0·57 for the Cl–O group overlap of $E$ symmetry, which is practically the same as the 0·6 given above. His values for the group overlap integrals in the four ions (Cl–O 0·57, S–O 0·52, P–O 0·46, Si–O 0·33) nicely parallel the bond shortenings ($0{\cdot}22_5$, 0·20, 0·17, and 0·13 Å). However, possibly misled by Wolfsberg and Helmholtz's misprint, which he repeats, he did not stress that only two of the five 3*d*-orbitals lead to strong π-bonding.

The key point of the present discussion is the assertion that in the $ClO_4^-$, $SO_4^{2-}$, $PO_4^{3-}$, and $SiO_4^{4-}$ ions two strongly π-bonding molecular orbitals are formed with the $3d_{x^2-y^2}$ and

[11] Moffitt, *Proc. Roy. Soc.*, 1950, *A*, **200**, 409.
[12] Wolfsberg and Helmholtz, *J. Chem. Phys.*, 1952, **20**, 837.
[13] Jaffé, *J. Phys. Chem.*, 1954, **58**, 185.

$3d_{z^2}$ orbitals of the central atom. The assertion is supported by the light it seems to throw on the sulphate, phosphate, and silicate structures discussed below. Whenever chloride, sulphur, phosphorus, or silicon is (approximately) tetrahedrally surrounded by ligands, these two *d*-orbitals are always of potential importance for π-bonding.

In the $XO_4$ ions each of the two 3*d*-orbitals is π-bonded to four oxygens, so that in valence-bond language each X–O bond has a π-bond order of $\frac{1}{4} + \frac{1}{4} = \frac{1}{2}$. In molecular-orbital language the bond order is $(\frac{1}{4})^{\frac{1}{2}} + (\frac{1}{4})^{\frac{1}{2}} = 1$, provided the bond is exactly homopolar. For the molecules we shall now go on to consider, we shall quote only valence-bond bond orders, partly because these can often be written down very easily and partly because there is quite a good correlation of them with molecular-orbital bond orders for aromatic molecules,[14] which suggests that it is unnecessary to make both sets of calculations in an introductory survey of the present kind.

*Application of the Hypothesis to a Series of Sulphates, Sulphamides, etc.*—Consider now a series of sulphur-containing molecules. The basic member of the series is the $SO_4^{2-}$ ion, in which the S–O length of valence-bond π-order $\frac{1}{2}$ is observed as 1·49 ± 0·01 Å. This is 0·20 Å shorter than the presumed single-bond length of 1·69 Å.

In the ethyl sulphate ion (Fig. 1) the original $p\pi'$-orbit of the fourth oxygen O(C) is utilised in the σ-bond to the ethyl group and in a lone pair in the SOC plane, but the other

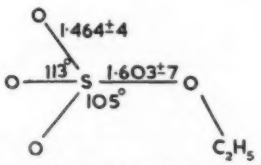



FIG. 1. $[(C_2H_5)SO_4]^-$ in $K(C_2H_5)SO_4$.

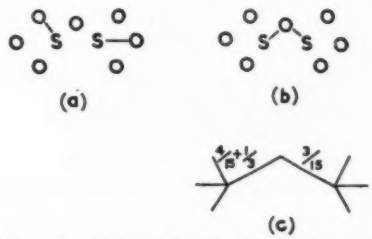



FIG. 2. Valence-bond structures and bond orders for $S_2O_7^{2-}$. (a) One of the 15 possible structures; (b) the excluded structure; (c) bond orders.

$p\pi$-orbit perpendicular to the SOC plane is still available for the π-system. If we assume that the energy of this orbit is unaltered when the ethyl group is attached, the π-bonding orbits may be written as

$$d \text{ with } \tfrac{1}{2}(p_1 + p_2 + p_3 + p_4)$$

and

$$d' \text{ with } (1/\sqrt{3})(p_1' + p_2' + p_3').$$

The π-bond order of S–O(C) would then be $\frac{1}{4}$; the length found by Jarvis and by Truter in potassium ethyl sulphate [15] is 1·603 ± 0·007 Å, which is correctly intermediate between 1·49 and 1·69 Å. The other three S–O bonds should contract because the *d'*-orbit is shared with only three oxygens. Thus the S–O bond order is $\frac{1}{2} + \frac{1}{4} = 0{\cdot}58$ and the actual length of 1·464 ± 0·004 Å is appropriately shorter than 1·49 Å. If we assume a linear bond-length–bond-order relation determined by 1·69 Å for a bond of π-order zero and 1·49 Å for order $\frac{1}{2}$, the theoretical lengths for ethyl sulphate are 1·59 and 1·46 Å.

The above argument has assumed that the $p_4$-orbit is of the same energy in $SO_4^{2-}$ and $RSO_4^-$. The formation of the σ-bond with R will draw electrons away from O(C), while the loss of the π-bond with S(3*d*) will increase the number of electrons on O(R). The balance of these effects cannot be estimated in a trivial approach, so it seems best to treat the actual S–O(C) bond length of 1·60 Å as evidence that the energy of $p_4$ is not greatly

[14] Cruickshank and Sparks, *Proc. Roy. Soc.*, 1960, *A*, **258**, 270.
[15] Jarvis, *Acta Cryst.*, 1953, **6**, 327; Truter, *ibid.*, 1958, **11**, 680.

altered and as an indication that this method of calculating bond orders may be reasonably applied to other sulphates.

In the $S_2O_7^{2-}$ pyrosulphate ion the bridge oxygen has a *p*-orbit, perpendicular to the SOS plane, which can link with a *d*-orbit on each sulphur and so give a π-bonding system running throughout the molecule; the other π-system, which uses the *d'*-orbits, remains in two distinct halves. For the π-system running through the molecule $4 \times 4 - 1 = 15$ valence-bond structures can be written if the one in which the bridge oxygen makes π-bonds to both sulphurs is excluded (Fig. 2). The bond orders are therefore S–O(bridge) $= 3/15 = 0{\cdot}20$ and S–O $= 4/15 + 1/3 = 0{\cdot}60$, corresponding to lengths 1·61 and 1·45 Å. The observed lengths from an accurate study of $K_2S_2O_7$ by Lynton and Truter [16] (Fig. 3) are $1{\cdot}645 \pm 0{\cdot}005$ Å and $1{\cdot}437 \pm 0{\cdot}004$ Å. These are correctly longer and shorter than the corresponding bonds in the ethyl sulphate. However, as a point

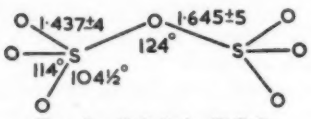



FIG. 3. $S_2O_7^{2-}$ in $K_2S_2O_7$.

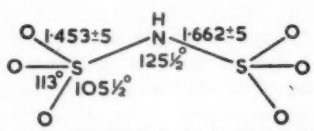



FIG. 4. $[NH(SO_3)_2]^{2-}$ in $K_2[(SO_3)_2NH]$.

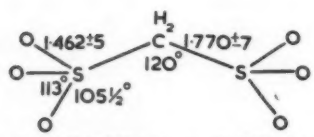



FIG. 5. $[CH_2(SO_3)_2]^{2-}$ in $K_2[(SO_3)_2CH_2]$.

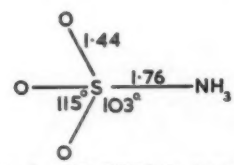



FIG. 6. $SO_3(NH_3)$ (±0·02 Å).

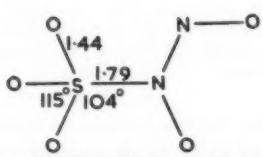



FIG. 7. $[SO_3N_2O_2]^{2-}$ in $(NH_4)_2SO_3N_2O_2$ (±0·02 Å).

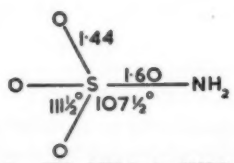



FIG. 8. $[SO_3{\cdot}NH_2]^-$ in $K[SO_3{\cdot}NH_2]$ (±0·03 Å).

of detail, the S–O(bridge) bond of 1·645 Å is slightly longer than the 1·61 Å expected for a bond of π-order 0·20.

If the bridge oxygen is replaced by NH, similar π-bonding might be expected since the *p*-orbit of nitrogen perpendicular to the S·NH·S plane will be available for π-bonding. The dimensions found [17] (Fig. 4) for the iminodisulphonate ion, in $K_2[(SO_3)_2NH]$, are very similar to those in the pyrosulphate. Indeed since the S–N bond of $1{\cdot}662 \pm 0{\cdot}005$ Å is only $0{\cdot}017 \pm 0{\cdot}007$ Å longer than the S–O(bridge) bond, whereas it might have been expected to be at least 0·05 Å longer on account of the different covalent radii of oxygen and nitrogen, there is a sense in which the S–N bond can be regarded as a relatively stronger π-bond than the S–O(bridge) bond.

A study of the isomorphous $K_2[(SO_3)_2CH_2]$ has just been completed by Dr. Mary R. Truter. On the present approach the carbon atom should have no *p*-orbit available for π-bonding and so the S–C bonds were expected to be pure single bonds of length at least

[16] Lynton and Truter, *J.*, 1960, 5112.
[17] Jeffrey and Jones, *Acta Cryst.*, 1956, **9**, 283; Cruickshank and Jones, unpublished work.

1·77 Å. [1·77 Å is the value found for S–C($H_3$) by Wheatley and his collaborators [18] in a series of dimethyl sulphones; 1·81 Å is the Schomaker–Stevenson value [7] for the S–C single bond.] The dimensions found (Fig. 5) are S–C = 1·770 ± 0·007 Å, S–O = 1·462 ± 0·005 Å, and ∠S–C–S = 120°. The S–C bond is thus similar to that in the dimethyl sulphones. In conformity with subsequent discussions of phosphate and silicate structures, the opening out of the S–C–S angle beyond 109½° (or the 112° or so found for C–C–C angles in paraffin chains) may be interpreted as due to the electrostatic repulsions of the two $SO_3^-$ groups. Discussion of the S–O length of 1·462 Å will be deferred to a later section on structures in which X is not surrounded by four π-bonding ligands.

The view that the S–N bond of 1·662 Å in the iminodisulphonate is a partial double bond can be proved, not merely by comparison with the pyrosulphate and the methylenedisulphonate, but also from the observation [19] that S–N bond length is 1·76 ± 0·02 Å in sulphamic acid $SO_3(NH_3)$, where the nitrogen has no orbitals available for π-bonding (Fig. 6). This value is close to the 1·74 Å for an S–N single bond given by the Schomaker–Stevenson rules.[7] A comparable S–N bond of 1·79 ± 0·02 Å is also found in the dinitrososulphite ion [20] [in $(NH_4)_2SO_3N_2O_2$], where the $p\pi$-orbit of the nitrogen is needed in the π-bonding system of the $N_2O_2$ group (Fig. 7). On the other hand, the results [20] for

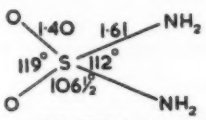



FIG. 9. $SO_2(NH_2)_2$ (±0·01 Å).

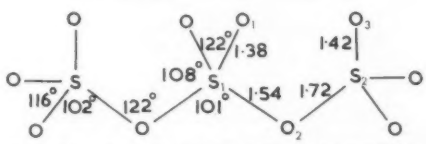



FIG. 11. $S_3O_{10}^{2-}$ in $(NO_2)_2S_3O_{10}$ (±0·05 Å).

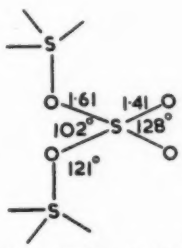



FIG. 10. $(SO_3)_\infty$ (±0·03 Å).

K[$SO_3$·$NH_2$], though not of great accuracy, show (Fig. 8) that the bonding in the sulphamate ion is analogous to that in the ethyl sulphate discussed above. (Jeffrey and Stadler, in their paper [20] on these last two structures, stressed that the large difference in S–N lengths showed that the bond in the sulphamate ion must have considerable double-bond character.)

In sulphonyl diamide, $SO_2(NH_2)_2$, whose structure has been determined by Trueblood and Mayer,[21] the two nitrogen atoms each have only one *p*-orbit available for the π-systems. The problem is whether one molecular orbital embraces the two oxygens and both nitrogens and the other just the two oxygens, or whether both embrace the nitrogens separately. This depends on the relative orientations of the $SNH_2$ planes. Group theory shows that the general rule is that, if the normals to these two planes are related by a two-fold rotation about the bisector of the NSN angle, then the two *p*-orbits on the nitrogens mate with the same *d*-orbit on the sulphur no matter what the relations of these normals to the OSO plane. To link with different *d*-orbits one of the nitrogen *p*-orbits must be rotated by 90° from these positions. Since in the actual crystal structure of sulphonyl diamide, the $NH_2$ groups are related by a two-fold axis through sulphur, both nitrogen *p*-orbits mate with the same *d*-orbit. Thus the S–N bonds are of order ¼ and the S–O bonds are of order ¼ + ½ = ¾. With additions

[18] Wheatley, *Acta Cryst.*, 1954, **7**, 68; Wheatley and Bullough, *ibid.*, 1957, **10**, 233; Daly, *J.*, 1961, 2801.
[19] Sass, *Acta Cryst.*, 1960, **13**, 320.
[20] Jeffrey and Stadler, *J.*, 1951, 1467.
[21] Trueblood and Mayer, *Acta Cryst.*, 1956, **9**, 628.

of 0·01 Å as approximate rotational-oscillation corrections to the values given by Trueblood and Mayer,[21] the observed lengths (Fig. 9) are 1·61 ± 0·01 Å for S–N, which is close to 1·60 ± 0·03 Å in the sulphamate ion, and 1·40 ± 0·01 Å for S–O. These S–O bonds are shorter than any others so far discussed and this is satisfactorily explained by their high bond order, which gives a theoretical length of 1·39 Å. The S–N bonds are within 0·01 Å of the S–O(C) bond of the same order in the ethyl sulphate. This very small difference parallels that discussed earlier between the S–N and S–O(bridge) bonds in $(SO_3)_2NH$ and $S_2O_7$. As the *p*-orbit on the nitrogen will be larger than that on the oxygen, the S(3*d*)–N(2*p*) overlap will be larger than the S(3*d*)–O(2*p*) overlap and this may lead to a stronger S–N π-bond.

Bond lengths rather similar to those in the sulphonyl diamide are predicted and found [22] in $(SO_3)_\infty$, where each tetrahedron is linked to two others (Fig. 10). The geometry of the chain is such that the *p*-orbits of the two bridging oxygens of each tetrahedron mate almost exactly (within 3°) with same *d*-orbit of the sulphur, so that a single π-system extends throughout the length of the molecule. The bond orders for the long and short

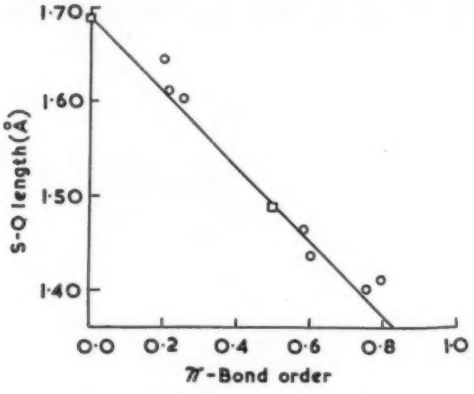



FIG. 12. S–O bond lengths and π-bond orders.

bonds are therefore 3/14 = 0·21 and 4/14 + ½ = 0·79, which correspond to lengths of 1·61 and 1·37 Å. These are sufficiently close to the observed values of 1·61 ± 0·03 and 1·41 ± 0·03 Å.

A rather approximate set of dimensions, with e.s.d.'s of about 0·05 Å, is available [23,24] for the trisulphate ion in $(NO_2)_2S_3O_{10}$ (Fig. 11). The π-bond orders are $S_1$–$O_1$ (16/56) + ½, $S_1$–$O_2$ 12/56, $S_2$–$O_2$ 11/56, $S_2$–$O_3$ (15/56) + 1/3. The predicted lengths in $S_3O_{10}^{2-}$ are then 1·38, 1·60, 1·61, and 1·45 Å, which show some similarity with the rather rough observed values of 1·38, 1·54, 1·72, and 1·42 Å.

Fig. 12 summarises this discussion of S–O bond lengths by plotting all the observed lengths, except those for the rather inaccurate $S_3O_{10}$, against the π-bond orders. The observed values lie gratifyingly close to the straight line drawn through 1·69 Å for order zero and 1·49 Å for order ½.

*Phosphates, Phosphoramides, etc.*—The hypothesis of double π-systems may be applied similarly to phosphates. Owing to an opening of the POP angle in some structures, the *p*-orbit lying in the POP plane has to be considered in addition to the perpendicular *p*-orbit. However, even when this is taken into account, the predictions of the hypothesis, though showing the right trends, are less satisfactory than with the sulphates. This discussion is hampered by the lack of an accurate analysis of an ion of the type $PO_3(OR)^{2-}$,

[22] Westrik and MacGillavry, *Acta Cryst.*, 1954, **7**, 764.
[23] Eriks and MacGillavry, *Acta Cryst.*, 1954, **7**, 430.
[24] Cruickshank, unpublished work.

whose place in the theoretical scheme corresponds to that of the ethyl sulphate ion. A surmise, based on the experimental results mentioned later for serine phosphate, is that the P–O(R) bond length in $PO_4R^{2-}$ is probably 1·62—1·63 Å. This is indeed about halfway between the bond length in the isolated phosphate ion (order $\frac{1}{2}$), which we shall take as $1{\cdot}54_5$ Å, and the P–O single bond, estimated by the Schomaker–Stevenson method (not of course observed), of 1·71 Å.

We note first that the S–N single bond of 1·76 ± 0·02 Å in sulphamic acid is paralled by the P–N single bond of 1·77 ± 0·02 found in the $PO_3^{2-}NH_3^+$ ion by Cruickshank's refinement [24] of Hobbs, Corbridge, and Raistrick's [25] results for sodium phosphoramide (Fig. 13). The Schomaker–Stevenson estimate for the P–N single bond is 1·76 Å, which is close to the experimental value and so tends to support the value of 1·71 Å for the (hypothetical) P–O single bond.

The most likely dimensions of the $P_4O_{10}$ molecule are shown in Fig. 14. These are optimum values derived from two gas-phase electron-diffraction studies [26,27] and from a new refinement [24] of the crystal structure data.[28] In this molecule each phosphate tetrahedron is joined to the three others, so that, since the three linked P–O bonds will have low bond orders, the unlinked P–O bond will have a high order and should be very short. This accords with the observed length of 1·40 ± 0·02 Å.

A calculation of the bond orders along the lines used for $S_2O_7$ is a little difficult because the symmetry of the molecule mixes the two systems of π-orbitals. For a molecule $R_3PO_4$

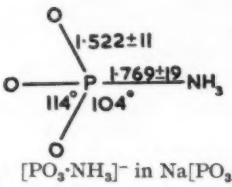



FIG. 13. $[PO_3{\cdot}NH_3]^-$ in $Na[PO_3{\cdot}NH_3]$.

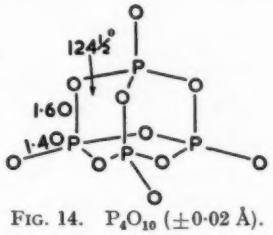



FIG. 14. $P_4O_{10}$ (±0·02 Å).

with a three-fold axis of symmetry, the bond orders may be estimated as 0·8 for P–O and 0·4 for P–O(R), since the first oxygen has two *p*-orbits available and the latter one. By analogy with $RSO_4$ and $S_2O_7$, the effect of replacing the R by other tetrahedra will be to accentuate the difference between the two types of bond. Extrapolation from calculations for the pairs of molecules $RXO_4$ and $X_2O_7$, $R_2XO_4$ and $X_3O_9$, $R_2XO_4$ and $X_4O_{12}$ to the pair $R_3PO_4$ and $P_4O_{10}$ suggests that the short and the long bonds in $P_4O_{10}$ will have a bond order ratio of roughly 3·0 : 1. Since the total bond order in any tetrahedron is 2·0, the bond orders are 1·00 and 0·33. If the P–O single bond is 1·71 Å and the bond of order $\frac{1}{2}$ is $1{\cdot}54_5$ Å, the expected bond lengths in $P_4O_{10}$ are therefore $1{\cdot}71 - 0{\cdot}16_5 \times (1{\cdot}0/0{\cdot}5) = 1{\cdot}38$ Å, and $1{\cdot}71 - 0{\cdot}16_5 \times (0{\cdot}33/0{\cdot}5) = 1{\cdot}60$ Å, which are close to the observed values of 1·40 and 1·60 Å. However, in the third form of phosphorus pentoxide,[29] which forms infinite sheets of $(P_2O_5)_\infty$, a new refinement [24] shows (Fig. 15) that the one unlinked and the three linked P–O bonds in each tetrahedron are 1·49 ± 0·02 and 1·56 ± 0·02 Å. The much smaller difference between the two types of bond is related to the opening of the POP bridging angles to an average of 145° as compared with 124° in $P_4O_{10}$. (This opening is caused at least partly by steric repulsions within a sheet.) Because of the opening, the P–O(bridge) bonds receive some π-character from the *p*-orbit in the POP plane as well as from the *p*-orbit perpendicular to the plane; the order of the unlinked P–O bond is then

[25] Hobbs, Corbridge, and Raistrick, *Acta Cryst.*, 1953, **6**, 621.
[26] Hampson and Stosick, *J. Amer. Chem. Soc.*, 1938, **60**, 1814.
[27] Akishin, Rambidi, and Zasorin, *Kristallografiya*, 1959, **4**, 360.
[28] de Decker and MacGillavry, *Rec. Trav. chim.*, 1941, **60**, 153.
[29] MacGillavry, de Decker, and Nijland, *Nature*, 1949, **164**, 448.

somewhat reduced. In the limit of $\angle POP = 180°$, both $p$-orbits on the oxygen perpendicular to the POP line would share fully in the two $\pi$-systems.

Fig. 16 shows the dimensions found [24,30] for the $P_2O_7^{4-}$ pyrophosphate ion in $Na_4P_2O_7,10H_2O$. The results are less accurate than those for the $S_2O_7^{2-}$ ion (Fig. 3), but the POP angle of $133\frac{1}{2}°$ is definitely larger than the SOS angle of 124°. The simple theory with just the one $p$-orbit on the bridge oxygen predicts, from the bond orders of 0·60 and 0·20, bond lengths of 1·51 Å and 1·64 Å. The observed bridge length of 1·61 Å is perhaps significantly less than the predicted 1·64 Å, but it is evident from the discussion of $P_4O_{10}$ and $P_2O_5$ that the actual difference of 0·10 Å between the short and the long bonds, as compared with the expected 0·13 Å, is about what might be expected when the POP angle is opened to $133\frac{1}{2}°$.

A slight opening also occurs in the $(PO_3^-)_\infty$ chain (Fig. 17) in rubidium metaphosphate.[24,31] The general stereochemistry of the chain is very similar to that of the $(SO_3)_\infty$ chain (Fig. 10); the mismatching of successive $p$-orbits with the intermediate phosphorus $p$-orbit is again only 3°. The simple theory gives bond orders of 0·79 and 0·21 for the short and the long bonds. The expected lengths are then 1·45 and 1·64 Å, which differ appreciably more than the observed $1·488 \pm 0·010$ and $1·616 \pm 0·010$ Å. The slight opening of the POP angle to 129° presumably allows the second $\pi$-system to play some

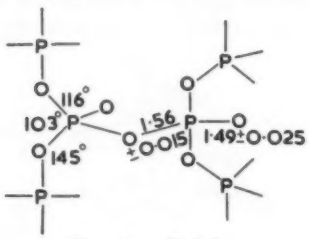



FIG. 15. $(P_2O_5)_\infty$.

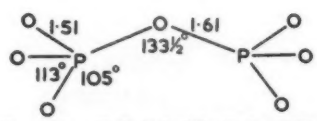



FIG. 16. $P_2O_7^{4-}$ in $Na_4P_2O_7,10H_2O$ ($\pm 0·015$ Å).

part in the bridging bonds, but the two types of bond are more equal in length than can probably be explained by this factor alone.

Figs. 18 and 19 show two other structures which contain doubly linked phosphate tetrahedra. Both present problems in interpretation. The triphosphate ion, which has a two-fold axis through $P_1$, is from the analysis of $Na_5P_3O_{10}$ by Davies and Corbridge [32] as refined by Cruickshank.[24] On the simple theory, with just one $p\pi$-orbit on oxygen, as in $S_3O_{10}$, the predicted lengths are 1·45, 1·64, 1·65, and 1·51 Å as compared with the observed 1·49, 1·61, 1·67, and 1·50 Å (e.s.d.'s $\pm$ 0·02 Å). The agreement in the outer tetrahedron is sufficiently close, but in the inner tetrahedron, whose dimensions are close to those in $(PO_3)_\infty$, the theory predicts too large a difference between the two bonds. It is no use appealing to an opening of the POP angle since this angle is only 122°. A conceivable explanation, which would apply to $(PO_3)_\infty$ also, is that the $\sigma$-character of the two bonds is different; since the $O_2'$–$P_1$–$O_2$ angle of 99° is halfway between $109\frac{1}{2}°$ and 90°, the $\sigma$-hybridisation of $P_1$–$O_2$ may tend towards $sp^3d^2$ from $sp^3$.

Two sets of dimensions (Fig. 19) are available for the $P_4O_{10}^{4-}$ tetrametaphosphate ion, one from the analysis of $(NH_4)_4P_4O_{12}$ by Romers, Ketalaar, and MacGillavry [33] as refined by Cruickshank [24] and the other from the analysis of $Na_4P_4O_{12},4H_2O$ by Ondik, Block, and MacGillavry.[34] In the ammonium salt the ion has $2/m$ symmetry by space-group requirements; in the sodium salt it has practically the same symmetry although this is not forced

[30] MacArthur and Beevers, *Acta Cryst.*, 1957, **10**, 428.
[31] Corbridge, *Acta Cryst.*, 1956, **9**, 308.
[32] Davies and Corbridge, *Acta Cryst.*, 1958, **11**, 315.
[33] Romers, Ketalaar, and MacGillavry, *Acta Cryst.*, 1951, **4**, 114.
[34] Ondik, Block, and MacGillavry, *Acta Cryst.*, 1961, **14**, 555.

by the space group. The dimensions of the ions in the two crystals agree within experimental error. The most interesting feature is that the lengths of the two types of P–O(bridge) bonds in the ring are different: 1·58 and 1·65 Å in the ammonium salt and 1·584 and 1·635 Å in the sodium salt. As the differences are in the same sense in both structures, it is clear that they are definite. *Prima facie*, the present theory might well explain this difference as due to different bond orders resulting from differences in geometrical environment. However, on examination of the way in which the various *d*- and *p*-orbits match up, the simple theory in fact suggests that one π-system is effectively continuous around the ring and that both P–O(bridge) bonds should have about the same bond order. Various possible refinements of the theory have proved equally unsuccessful.*

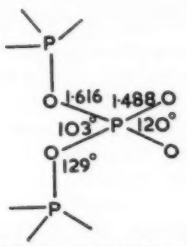



FIG. 17. $(PO_3^-)_\infty$ in $RbPO_3$ (±0·010 Å).

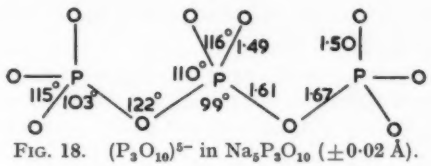



FIG. 18. $(P_3O_{10})^{5-}$ in $Na_5P_3O_{10}$ (±0·02 Å).

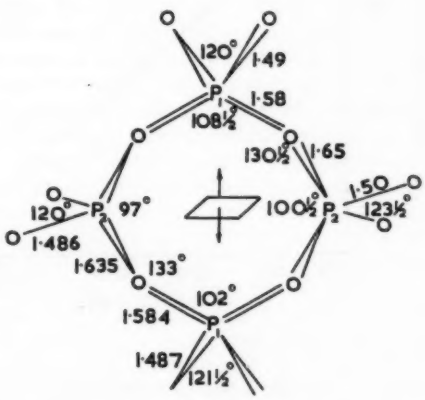



FIG. 19. The tetrametaphosphate ion. Dimensions at upper right from $(NH_4)P_4O_{12}$ (±0·03 Å), at lower left from $Na_4P_4O_{12}.4H_2O$ (±0·016 Å).

Leaving aside this difficulty, we note that the averages of 1·61 Å for the two P–O(bridge) bonds and 1·49 Å for the P–O(unlinked) bonds are practically the same as those for the corresponding bonds in the doubly linked tetrahedra in $(PO_3)_\infty$ and $P_3O_{10}$. These lengths, together with linked and unlinked OPO angles of about 100° and 120°, are therefore consistent structural features. This consistency is not upset by the fact that in $P_3O_{10}$ the bridging *d*-orbit is mainly $d_{x^2-y^2}$ $(0{\cdot}98d_{x^2-y^2} + 0{\cdot}18d_{z^2})$, while in $(PO_3)_\infty$ it is largely $d_{z^2}$ $(0{\cdot}38d_{x^2-y^2} + 0{\cdot}93d_{z^2})$, where local axes have been chosen so that the *z*-axis is the bisector of the O(bridge)–P–O(bridge) angle and the *x*- and *y*-axes are at ±45° to that plane.

Fig. 20 collects together all the results for the P–O bonds mentioned in this section, except those for $(P_2O_5)_\infty$ in which the opening of the P–O–P angles has such a marked effect. Despite the difficulties in $P_4O_{12}$ and the effects of the slight opening out of the P–O–P angles in some structures, the observed P–O lengths cluster quite close to the theoretical line based on unopened angles.

*Silicon–Oxygen Bonds.*—The chief difficulty in a discussion of the lengths of Si–O bonds is the paucity of accurate results. Though the crystal structures of many silicates have been worked out, the number of these with relatively pure chemical composition and with

* See note added in proof at end of paper.

bond lengths accurate even to 0·05 Å is quite small. The most remarkable feature of the available results is that practically all the known Si–O distances are within 0·03 Å of 1·63 Å. The known spread of Si–O distances is thus much smaller than the spread of P–O or S–O distances, which are 1·40—1·67 and 1·40—1·64 Å, respectively. (The details of Si–O bonds in molecules in which silicon is not linked to four oxygens will be considered later, but even for these the distances are close to 1·63 Å.) Some reasons for this smaller spread will emerge shortly, but it is probable that the more varied Si–O bonds will be found in suitable structures.

No results are available for ions of the type $RSiO_4^{3-}$, $R_2SiO_4^{2-}$, or $R_3SiO_4^{-}$, but an electron-diffraction study [35] of tetramethyl silicate gives Si–O = 1·64 ± 0·03 Å (and ∠Si–O–C = 113° ± 2°). Since each oxygen has only one *p*-orbit available for $\pi$-bonding, the Si–O bonds will be of order ½ and should therefore be, as they are, of similar length to those in a $SiO_4^{4-}$ group.

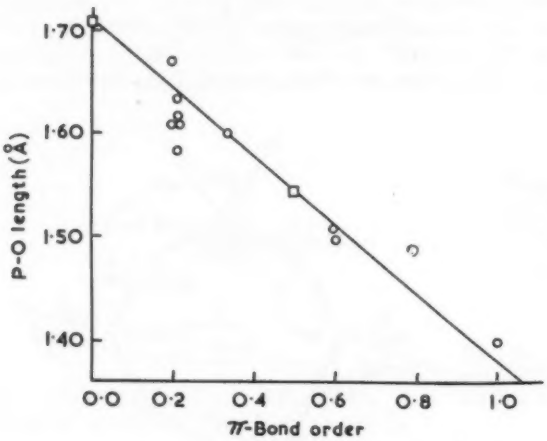
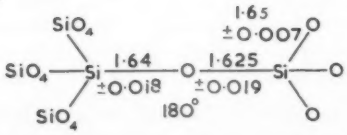



FIG. 20. P–O bond lengths and $\pi$-bond orders.

(The indication corresponding to $\pi$-bond order 0·8 is the superposition of three circles.)

FIG. 21. $[Si_5O_{16}]^{12-}$ in zunyite.




The equalisation of bond orders in linking and non-linking X–O bonds by the opening of the X–O–X angles reaches a limit in some of the silicates. In thortveitite,[36] $Sc_2Si_2O_7$, the $Si_2O_7$ pyrosilicate ion has a linear Si–O–Si bridge with an inner Si–$O_1$ bond of 1·607 ± 0·007 Å and an outer Si–$O_2$ bond of 1·626 ± 0·012 Å. These dimensions are similar to those reported in two-dimensional work on seidozerite [37] (∠Si–O–Si 180°, inner Si–O 1·63 Å, outer Si–O 1·635 Å) and are paralleled in Kamb's three-dimensional work on zunyite [38] where the $Si_5O_{16}$ group (Fig. 21) has linear Si–O–Si links and Si–O lengths of 1·64 ± 0·018, 1·625 ± 0·019, and 1·65 ± 0·007 Å.

In pyrosilicate groups with ∠Si–O–Si = 180°, the bridge oxygen $O_1$ will have two *p*-orbits available for $\pi$-bonding and so may join fully in both $\pi$-systems. On the simple picture the $\pi$-bond orders are 2/5 for the inner bonds and 8/15 for the outer bonds. With 1·76 Å for a single bond and 1·63 Å for a bond of order ½, the predicted lengths are 1·656

[35] Yamasaki, Kotera, Yokoi, and Ueda, *J. Chem. Phys.*, 1950, **18**, 1414.
[36] Cruickshank, Lynton, and Barclay, *Acta Cryst.*, in the press.
[37] Simonov and Belov, *Kristallografiya*, 1959, **4**, 163.
[38] Kamb, *Acta Cryst.*, 1960, **13**, 15.

and 1·621 Å. To a rough approximation the bonds ought to be of about equal length, which is what is observed, but in detail the inner bond ought to be slightly the longer, which is not correct for thortveitite. The observations cannot be explained either by reversion to a simple electrostatic picture of the old style, in which both the Si–O π-bonds and the partial covalent character of the inter-ionic Sc–O bonds are ignored. In such an approach, with the crystal treated as an array of discrete $Sc^{3+}$ and $Si_2O_7^{6-}$ ions and with 50% ionic character for the Si–O σ-bonds,[39] a simple electrostatic calculation for an isolated $Si_2O_7^{6-}$ group suggests that, with reasonable force constants, the outer Si–O bonds should be of the order of 0·1 Å shorter than the inner bonds. However, as discussed by Cruickshank, Lynton, and Barclay,[36] some details of the packing together of the pyrosilicate groups in the crystal seem intelligible only with reduced formal charges on the outer oxygens. These reduced charges (and consequent reduced charges on the scandium and $Si_2O_7$ ions) would fit with a slight covalent character for the Sc–O bonds and so with Pauling's electroneutrality principle. It would then be possible for the net charge on the inner oxygen (say, −0·8) to be greater than the charges (say, −0·5) on the outer oxygens, so that the near equality of the Si–O bonds in thortveitite could be explained by a balance of an electrostatic effect, tending to make the inner bonds the shorter, and the π-bond effect, tending to make the inner bonds the longer.

Although the details of some of the structures are a little doubtful, crystals with $Si_2O_7$ groups show variations of the Si–O–Si angles from the 180° of thortveitite and seidozerite down to about 135° in hemimorphite [40] and lawsonite.[41] The evident dependence of the structure of the $Si_2O_7$ group on crystal environment is in keeping with the above remarks on the importance of the partial covalent character of the inter-ionic bonds. (Indeed, with any plausible bending-force constant for oxygen, it is easily shown that, if an isolated $Si_2O_7$ group has a total charge of −6, the electrostatic forces are sufficient to compel the Si–O–Si link to be linear.) The reported Si–O distances for the pyrosilicate groups in hemimorphite or lawsonite are not sufficiently accurate for comparison to be made with theoretical estimates of these distances.

Si–O–Si angles of around 135° have been found in several $(SiO_3)_\infty$ chains, but unfortunately no really accurate result seems available. The two-dimensional least-squares studies of clinoenstatite and pigeonite by Morimoto, Appleman, and Evans,[42] together with the older results for diopside,[43] show that Si–O(bridge) bonds tend to be about 0·05 Å larger than Si–O(unlinked) bonds. If the Si–O–Si angles were about 120°, the bond orders quoted earlier for $(SO_3)_\infty$ imply a difference of about 0·14 Å (1·70 and 1·56 Å). The smaller actual difference is presumably partly due to the opening of the Si–O–Si angles to about 135° and partly to the same (?electrostatic) effect as seems to operate for the inner and the outer bonds in thortveitite. In $Na_2SiO_3$ the bonds are reported [44] as 1·68 and 1·57 Å, but the accuracy of these results cannot be high since the residual $R$ is 27%. An accurate analysis of a structure of this type is very desirable.

Si–O bond lengths with e.s.d.'s of 0·01 or 0·02 Å have been obtained by Meier [45] for the $Si_3O_{10}$ group in natrolite, $Na_2Al_2Si_3O_{10}$. They all lie in the range 1·60—1·65 Å. In the crystal structure there are also numerous Al–O bonds of length about 1·75 Å, which are not very dissimilar in character to the Si–O bonds. Consequently the $Si_3O_{10}$ group cannot be considered as separate an entity as an $S_3O_{10}$ group and no simple predictions of its bond lengths can be made, though clearly all the Si–O bonds will tend to be approximately equal in length as every oxygen belongs either to two silicon tetrahedra or to one silicon and one aluminium tetrahedron.

[39] Pauling, " The Nature of the Chemical Bond," Cornell Univ. Press, 3rd edn., 1960.
[40] Barclay and Cox, *Z. Krist.*, 1960, **113**, 23.
[41] Rumanova and Skipetrova, *Doklady Akad. Nauk S.S.S.R.*, 1959, **124**, 324.
[42] Morimoto, Appleman, and Evans, *Z. Krist.*, 1960, **114**, 120.
[43] Warren and Bragg, *Z. Krist.*, 1928, **69**, 168.
[44] Grund and Pizy, *Acta Cryst.*, 1952, **5**, 837.
[45] Meier, *Z. Krist.*, 1960, **113**, 430.

Accurate results are available for two forms of silica $(SiO_2)_\infty$, α-quartz [46] and coesite.[47] In α-quartz the Si–O–Si angle is 144°, in coesite there is one angle of 180° and four in the range 139—148°. The spread of angles in this one structure may be compared with the similar spread in the various structures with pyrosilicate groups. In both α-quartz and coesite the Si–O distances are all close to 1·61 Å. In each structure the Si–O π-bond orders will be approximately $\frac{1}{2}$, irrespective of the details of the linking of the π-systems through the *p*-orbits of the oxygens. The observed 1·61 Å is close to the 1·63 Å, which has been noticed both as the general average for Si–O distances and as the length of the bonds (also of order $\frac{1}{2}$) in the $SiO_4$ group itself, though perhaps there is again the tendency for an external bond, as in $SiO_4$, to be slightly longer than an internal bond of the same order.

The present π-bonding theory suggests an important difference between α- and β-quartz. In β-quartz,[48] of which an accurate modern determination seems very desirable, each silicate tetrahedron has three two-fold axes of symmetry. Consequently, on the four oxygens the *p*-orbits, which are normal to the Si–O–Si planes, all match the same silicon *d*-orbit, so that one π-system plays a dominant rôle in the structure. In α-quartz, where each tetrahedron has a single two-fold axis, the geometry shows that the *p*-orbits on the two independent types of oxygen are 73°, *i.e.*, nearly 90°, out of phase for overlapping the same silicon *d*-orbital. Consequently, both π-systems, using two essentially distinct *d*-orbits, play an equal rôle in the structure of α-quartz. In both systems a small part of the π-bonding will arise from the *p*-orbit which bisects the 144° Si–O–Si angle.

It was remarked earlier that the known spread of Si–O distances about 1·63 Å is very small. This seems partly due to the accident that most of the structures studied have involved linked silicate tetrahedra, in which the opening of the Si–O–Si angles has tended to equalise the π-bond orders. A structure such as, say, $R_2SiO_4^{2-}$ might therefore offer a better chance of finding more varied Si–O bonds. Here the π-bond orders will be $\frac{1}{4}$ for Si–O(R) and $\frac{3}{4}$ for Si–O.

X–O *Bonds when* X *is not Surrounded by Four* π*-Bonding Ligands.*—In many sulphones, $R_2SO_2$, S–O lengths close to 1·43 Å (and O–S–O angles of about 120°) have been found. The bonding in such systems has been discussed by Moffitt [11,49] but, as Jaffé has pointed out,[13] he did not realise that the sulphur *d*-orbit of $a_1$-symmetry, corresponding to the present $d_{z^2}$-orbital, can be involved in π-bonding to the oxygens. In any molecule where sulphur is surrounded by four ligands in an approximately tetrahedral arrangement, π-bonding can occur between suitable ligand orbitals and the sulphur orbitals, $d_{z^2-y^2}$ and $d_{z^2}$ (with some admixture of $d_{xy}$ if the angles are distorted), in the same kind of way as described for the sulphate ion. On a blind application of the present treatment to the sulphones, S–O bonds much shorter than the observed 1·43 Å would be expected, since the bond orders are $\frac{1}{2} + \frac{1}{2} = 1$, which implies a length of about 1·3 Å. The relatively small contraction from the 1·49 Å of the sulphate ion may be ascribed to the smaller electronegativity of a group R than of oxygen and to the asymmetry of the π-bonding about sulphur, so that the effective nuclear charge $Z_{eff}(3d)$ for the 3*d*-orbitals is lowered with a loss of bonding strength. In the sulphonates, $R{\cdot}SO_3^-$, lengths of 1·44 ± 0·02, 1·462 ± 0·005, and 1·45 ± 0·01 Å are reported for sulphamic acid,[19] methylenedisulphonate,[50] and sodium naphthionate.[51] These are intermediate between the 1·49 Å of the sulphate ion and the 1·43 Å of the sulphones.

If a group R in one of the tetrahedral positions of a sulphone is replaced by a lone pair to give $R{\cdot}SO_2^-$, $Z_{eff}(3d)$ should be considerably reduced and in sodium hydroxymethanesulphinate [50,52] the S–O bonds are duly found to be lengthened from 1·43 to 1·51 Å (though

[46] Alexander and Smith, personal communication.
[47] Zoltai and Buerger, *Z. Krist.*, 1959, **111**, 129.
[48] Bragg and Gibbs, *Proc. Roy. Soc.*, 1925, *A*, **109**, 405.
[49] Koch and Moffitt, *Trans. Faraday Soc.*, 1951, **47**, 7.
[50] Truter, unpublished work.
[51] Brown and Corbridge, unpublished work.
[52] Truter, *J.*, 1955, 3064.

some of this lengthening might be due to a change in the σ-bond strength, since the S–C bond of 1·83 Å is also rather long).

In a similar way in the series $ClO_4^-$, $ClO_3^-$, $ClO_2^-$, and $ClO^-$, where lone pairs successively replace oxygens in the tetrahedron, the bond lengths [3,53] (1·46, 1·46 ± 0·01 + some rotational correction, 1·57 ± 0·03 Å, and ?) are a balance between the increasing bond order of the Cl–O bonds ($\frac{2}{4}$, $\frac{2}{3}$, $\frac{2}{2}$, $\frac{2}{1}$) and the successively lowered $Z_{eff}$ for the Cl(3*d*) orbitals.

Some similarities to the sulphonates and sulphones can be observed in structures containing phosphorus. As compared with the $1{\cdot}54_5$ Å of $PO_4^{3-}$, values observed are about 1·52 Å for $R{\cdot}PO_3^{2-}$ [1·52 ± 0·01 in [24,25] $PO_3NH_3^-$, 1·51 ± 0·05 in [54] $HPO_3^{2-}$, and a mean of 1·53 ± 0·02 Å for P–O and P–O(H) in [55] $HPO(OH)_2$] and 1·50 ± 0·02 Å for $R_2PO_2^-$ [the hypophosphite ion [55] in $Ca(PO_2H_2)_2$]. In $P_4O_6$, as compared with $P_4O_{10}$, the effect of replacing the four outer oxygens by lone pairs is to increase the P–O length [26] from 1·60 to 1·65 ± 0·02 Å.

The closeness of Si–O lengths in silicates to 1·63 Å has already been noted. The same length (1·633 ± 0·001 Å) is found [56] in an accurate electron-diffraction study of disilyl ether, $(SiH_3)_2O$, where the Si–O–Si angle is 144° ± 1°. Similar, but much less accurate, dimensions had been found in earlier studies [35] of $[(CH_3)_3Si]O$ and $(Cl_3Si)_2O$. The opening of the Si–O–Si angle beyond 109½° necessarily implies π-bonding and/or electrostatic effects. On the present view, the oxygen *p*-orbit perpendicular to the Si–O–Si plane will join in π-bonds, while the *p*-orbit bisecting the angle will also play some part because the angle is so large. Lengths near to 1·63 Å are also found in the crystal structure [57] of $(C_2H_5)_2Si(OH)_2$ and in the $-O{\cdot}Si(CH_3)_2{\cdot}O-$ groupings [58-60] in spirosiloxane, $[(CH_3)_2SiO]_4$, and $[(CH_3)_2SiO]_3$. On the present approach, the approximate equality of all these Si–O distances is to be regarded as an accident of a balance of the varying π-bond orders with the varying $Z_{eff}$(3*d*) and electrostatic forces.

As Craig *et al.*[61] remarked, evidence of the ability of Si(3*d*) orbitals to form π-bonds with nitrogen may be found [62] from $(H_3Si)_3N$, where the co-planar Si–N bonds of 1·71 ± 0·02 Å are 0·06 Å shorter than the expected Si–N single-bond length.

*Effect of Attached Hydrogen.*—It seems to be a general rule for *crystals* that, when hydrogen is attached to sulphate or phosphate groups, the bond lengths are roughly halfway between those for the ion without the proton and for the ion with a group R attached. Thus in mercallite [63] $KHSO_4$, where the OH · · · O hydrogen bonds are 2·62 Å long, an appreciable refinement [24] shows that the average dimensions from the two $HSO_4^-$ ions are S–O(H) = 1·56 and S–O = 1·47 ± 0·015 Å. The difference between the short and the long bonds is 0·09 Å, compared with the larger difference of 0·14 Å in ethyl sulphate.

In the low-temperature form [64] of $KH_2PO_4$, where the hydrogen bonds are 2·49 Å long, P–O(H) = 1·58 and P–O = 1·51 Å, with a difference of 0·07 Å; in phosphoric acid [65] $H_3PO_4$, with hydrogen bonds 2·50—2·59 Å long, the lengths are 1·57 and 1·52 with a difference of only 0·05 ± 0·02 Å. The distinction between attached hydrogen and attached R is beautifully illustrated by the analysis of serine phosphate [66] (Fig. 22), where the phosphate group has both hydrogen and R attached, and the hydrogen bond is 2·55 Å

[53] Gillespie, Sparks, and Trueblood, *Acta Cryst.*, 1959, **12**, 867.
[54] Corbridge, *Acta Cryst.*, 1956, **9**, 991.
[55] Loopstra, Thesis, Amsterdam, 1958.
[56] Bastiansen and Traetteberg, personal communication.
[57] Kakudo and Watase, *J. Chem. Phys.*, 1953, **21**, 167.
[58] Roth and Harker, *Acta Cryst.*, 1948, **1**, 34.
[59] Peyronel, *Atti Accad. naz. Lincei, Rend.*, 1954, **16**, 231.
[60] Steinfink, Post, and Fankuchen, *Acta Cryst.*, 1955, **8**, 420.
[61] Craig, Maccoll, Nyholm, Orgel, and Sutton, *J.*, 1954, 332.
[62] Hedberg, *J. Amer. Chem. Soc.*, 1955, **77**, 6491.
[63] Loopstra and MacGillavry, *Acta Cryst.*, 1958, **11**, 349.
[64] Bacon and Pease, *Proc. Roy. Soc.*, 1955, *A*, **230**, 359.
[65] Furberg, *Acta Chem. Scand.*, 1955, **9**, 1557.
[66] McCallum, Robertson, and Sim, *Nature*, 1959, **184**, 1863.

long. Here P–$O_1$(R) = 1·61 Å, while the P–$O_4$(H) bond of 1·56 ± 0·01 Å is definitely shorter. An examination of the geometry of the molecule shows that the *p*-orbit of $O_4$(H) is about 60° out of alignment with that *d*-orbit of P which mates with the *p*-orbit of $O_1$(R). Consequently the bond order of P–O(R) is somewhat less than ½, which would be the value for an ion $R_2PO_4^-$ with a two-fold axis of symmetry. It is for this reason that the P–O(R) bond length in $R{\cdot}PO_4^{2-}$, discussed earlier, is estimated as a little larger than 1·61 Å, say 1·62—1·63 Å.

The dimensions of dibenzyl hydrogen phosphate are shown in Fig. 23. These differ from those given by Dunitz and Rollett,[67] after their three-dimensional anisotropic SFLS

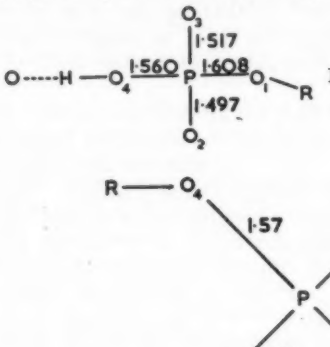



FIG. 22. Serine phosphate (±0·01 Å).

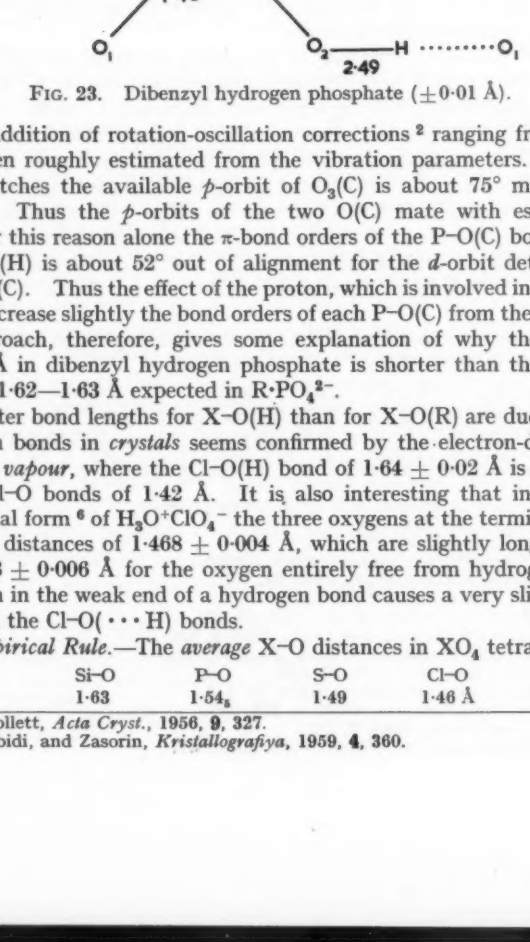



FIG. 23. Dibenzyl hydrogen phosphate (±0·01 Å).

analysis, by the addition of rotation-oscillation corrections [2] ranging from 0·006 to 0·015 Å which have been roughly estimated from the vibration parameters. The phosphorus *d*-orbit which matches the available *p*-orbit of $O_3$(C) is about 75° mismatched for the *p*-orbit of $O_4$(C). Thus the *p*-orbits of the two O(C) mate with essentially different *d*-orbitals, and for this reason alone the $\pi$-bond orders of the P–O(C) bonds are at least ⅓. The *p*-orbit of $O_2$(H) is about 52° out of alignment for the *d*-orbit determined by $O_4$(C) and 45° out for $O_3$(C). Thus the effect of the proton, which is involved in a 2·49 Å hydrogen bond, will be to increase slightly the bond orders of each P–O(C) from the ⅓ already derived. The present approach, therefore, gives some explanation of why the average P–O(C) distance of 1·56 Å in dibenzyl hydrogen phosphate is shorter than the 1·61 Å in serine phosphate or the 1·62—1·63 Å expected in $R{\cdot}PO_4^{2-}$.

That the shorter bond lengths for X–O(H) than for X–O(R) are due to the formation of short hydrogen bonds in *crystals* seems confirmed by the electron-diffraction study [68] of perchloric acid *vapour*, where the Cl–O(H) bond of 1·64 ± 0·02 Å is some 0·2 Å longer than the three Cl–O bonds of 1·42 Å. It is also interesting that in the ordered low-temperature crystal form [6] of $H_3O^+ClO_4^-$ the three oxygens at the termini of the hydrogen bonds have Cl–O distances of 1·468 ± 0·004 Å, which are slightly longer than the Cl–O distances of 1·443 ± 0·006 Å for the oxygen entirely free from hydrogen bonds. Thus, even participation in the weak end of a hydrogen bond causes a very slight loss of double-bond character in the Cl–O(···H) bonds.

*A Simple Empirical Rule.*—The *average* X–O distances in $XO_4$ tetrahedra are about:

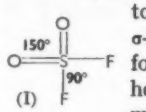
| Si–O | P–O | S–O | Cl–O |
|---|---|---|---|
| 1·63 | 1·54$_5$ | 1·49 | 1·46 Å |

[67] Dunitz and Rollett, *Acta Cryst.*, 1956, **9**, 327.
[68] Akishin, Rambidi, and Zasorin, *Kristallografiya*, 1959, **4**, 360.

X–O bonds which involve oxygen linked to another atom or to another tetrahedron may lengthen by amounts up to ~0·15 Å but the other X–O bonds in the tetrahedron contract so as to preserve the average.

*Bonds to Fluorine.*—The tetrahedral molecule $SiF_4$ is isoelectronic with the orthosilicate ion and has a Si–F bond length [69] of 1·56 ± 0·02 Å. This is 0·13 Å shorter than the value predicted for a Si–F single bond by the Schomaker–Stevenson method; thus it seems that the fluorine $2p\pi$- and $2p\pi'$-orbitals engage in some π-bonding with the silicon $d_{z^2}$- and $d_{x^2-y^2}$-orbitals.

Sulphonyl fluoride, $SO_2F_2$, is isoelectronic with $SO_4^{2-}$ and has the dimensions [70] S–O 1·405, S–F 1·530 Å, ∠O–S–O 124°, ∠F–S–F 96°. As compared with the sulphones, $R_2SO_2$, where R is a hydrocarbon residue, the effect of fluorine is to contract the S–O distance a little, from 1·43 to 1·405, and to open the angle from 120°. We may regard the structure of sulphuryl fluoride as intermediate between that of an exactly tetrahedral molecule, in which fluorines participate in the π-bonding in a similar, but reduced, fashion to the oxygens, and one based on a sulphur atom with six octahedral ($sp^3d^2$) σ-orbits, which would give the configuration (I) with the S=O double bonds formed from two bent σ-bonds. The Schomaker–Stevenson value from tetrahedral radii for the S–F single bond is 1·625 Å; an old study [71] of the octahedral molecule sulphur hexafluoride gives S–F 1·58 ± 0·03 Å. The value of 1·530 Å in sulphuryl fluoride therefore indicates some double-bond character in the S–F bond.



(I)

The isoelectronic molecule $PF_3O$ is even less distorted from the tetrahedral configuration. Here ∠F–P–F is reported [72] as 106°, P–F as 1·52 Å, and P–O as 1·48 Å. It is noticeable that both bonds are shorter than the 1·54 Å for the P–O in an orthophosphate ion and that the P–F bond is decidedly shorter than 1·65 Å for the Schomaker–Stevenson single bond.

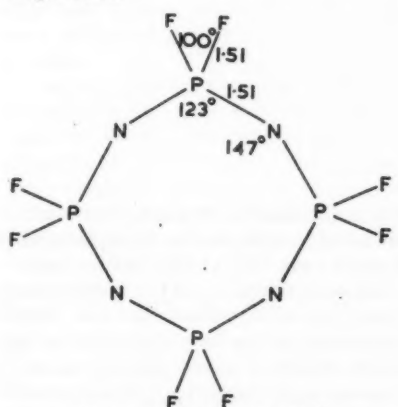


FIG. 24. $[PNF_2]_4$ (±0·01 Å).

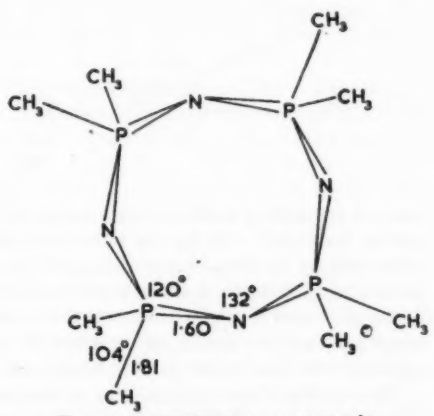


FIG. 25. $[PN(CH_3)_2]_4$ (±0·005 Å).

We now turn to the isoelectronic pair of phosphonitrilic molecules $[PNF_2]_4$ and $[PN(CH_3)_2]_4$, whose structures have been recently determined [73] with some precision by *X*-ray methods (Figs. 24 and 25). In the difluoro-tetramer, which has a planar eight-membered ring, the *p*-orbits of the nitrogens perpendicular to the plane can match exactly with the phosphorus $d_{x^2-y^2}$-orbitals (these are the $d_{xz}$-orbitals in Craig's system of axes [74]),

[69] Atoji and Lipscomb, *Acta Cryst.*, 1954, **7**, 597.
[70] Lide, Mann, and Fristrom, *J. Chem. Phys.*, 1957, **26**, 734.
[71] Brockway and Pauling, *Proc. Nat. Acad. Sci. U.S.A.*, 1933, **19**, 68.
[72] Hawkins, Cohen, and Koski, *J. Chem. Phys.*, 1952, **20**, 528.
[73] McGeachin and Tromans, *J.*, in the press; Dougill, *J.*, 1961, 5471.
[74] Craig, *J.*, 1959, 997.

while owing to the large P–N–P angle of 147° some further $\pi$-bond character in the P–N bonds can be obtained from the matching of the $p$-orbit, which bisects the P–N–P angle, with the phosphorus $d_{z^2}$-orbitals (to which a little $d_{xy}$ may be added to compensate for the distortions from tetrahedral angles). The P–F distance of 1·51 Å in this tetramer is similar to the P–F distance of 1·52 Å in $PF_3O$, so that it also shows some $\pi$-bond character.

When the fluorines of sulphuryl fluoride are replaced by methyl groups the S–O distance increases; it is therefore reasonable that the P–N distances in $[PN(CH_3)_2]_4$ are longer than those in $[PNF_2]_4$, as is indeed found. However, the ring of the dimethyl-tetramer is considerably puckered and it might therefore seem that the $\pi$-bonding systems would be very different. The relevant point is the measure of mismatching between the $p$-orbits on successive nitrogens, perpendicular to the P–N–P planes, and the intermediate $d$-orbits. In the dimethyl-tetramer, which has $\bar{4}$ symmetry, an orbit $0{\cdot}73\,d_{x^2-y^2} + 0{\cdot}69d_{z^2}$ is only $\pm 11\frac{1}{2}°$ mismatched to the principal $p$-orbits of the adjoining nitrogens. Thus the introduction of the $d_{z^2}$-orbital ($d_{y^2}$ in Craig's axes) allows the principal $\pi$-bond system to retain much of its energy despite the puckering of the molecule. The increase of the P–N

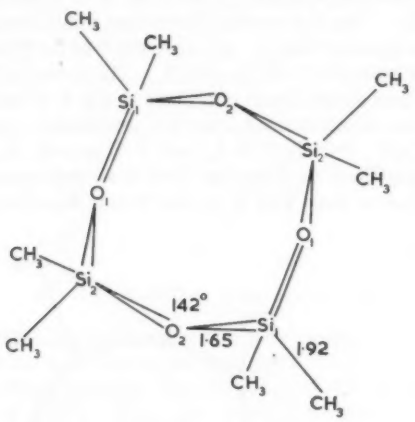



FIG. 26. $[SiO(CH_3)_2]_4$ ($\pm 0{\cdot}03$ Å).

length from 1·51 Å in the difluoro-tetramer to 1·60 Å in the dimethyl-tetramer may therefore be correlated with (*a*) the inevitable direct increase of lengths due to the replacement of fluorine by methyl, (*b*) the closing of the P–N–P angle from 147° to 132°, with a consequent loss of strength in the minor $\pi$-bond system, and (*c*) the slight ($\pm 11\frac{1}{2}°$) mismatching of the principal $p$-orbits. These effects are, of course, not independent, and the above account is not so much an explanation of the structure of the two molecules as an indication of some of the factors which will have to be considered in any full explanation.

It is perhaps appropriate here to mention the isoelectronic $[SiO(CH_3)_2]_4$, which is also heavily puckered [60] (Fig. 26). In this the orbital $0{\cdot}78\,d_{x^2-y^2} + 0{\cdot}63d_{z^2}$ on $Si_1$ is $\pm 14°$ mismatched to the adjacent oxygens, while the orbital $-0{\cdot}17d_{x^2-y^2} + 0{\cdot}98d_{z^2}$ on $Si_2$ is $\pm 21°$ to the adjacent oxygens. It is perhaps not surprising that these mismatchings mismatched are a little greater than in $[PN(CH_3)_2]_4$, since the average Si–O–Si angle of 142° will allow the second $\pi$-system to play a proportionately larger rôle than in phosphonitrile tetramer with its P–N–P angle of 132°.

*Discussion.*—Apart from the initial discussion of bonding in the $XO_4$ ions, the theory presented in this paper has been deliberately kept at a very low mathematical level. The reason for this has been that the simple geometrical ideas of the double $\pi$-bonding system seem to go a long way in explaning the general features of the structures. The simple picture has its obvious shortcomings, but it has seemed more important first to codify the experimental results and to see how they fit a simple scheme, than to embark

prematurely on a detailed theoretical treatment of a particular molecule. The details of the present semiempirical classification cannot possibly all be correct, but the overall correlation seems sufficiently compelling to indicate that some of the ideas must be integral features of any fuller theory.

It is not only the theoretical side which needs more attention; much vital experimental information is still lacking. Some of the wanted key structures have been mentioned at appropriate points. As one illustration of the need for further experimental work, consider the $X_2O_7$ ions. We have quoted the dimensions of the $Si_2O_7$ group [36] in thortveitite (inner X–O = 1·607 ± 0·007 Å, outer X–O = 1·626 ± 0·012 Å and ∠X–O–X = 180°), the $P_2O_7$ group [24] in $Na_4P_2O_7,10H_2O$ (1·61 ± 0·015 Å, 1·51 ± 0·015 Å, 133½°), and the $S_2O_7$ group [16] in $K_2S_2O_7$ (1·645 ± 0·005 Å, 1·437 ± 0·004 Å, 124°). To these may be added the results of a recent Russian gas-electron-diffraction study [68] of $Cl_2O_7$ (1·725 ± 0·03 Å, 1·424 ± 0·01 Å, 115 ± 5°). It is tempting to be satisfied with noting that the differences of the inner and the outer bonds in these four groups are very close to 0·0, 0·1, 0·2, and 0·3 Å and to correlate this with the change of angle from 180° to 133½°, 124°, and 115°, a correlation which can be related to the decreasing rôle of the second π-system in the inner bond as the X–O–X angle falls below 180°. To do only this is to oversimplify the situation. First, in the pyrosilicates the Si–O–Si angle can go as low as 135°, yet no accurate bond lengths are available for such structures (indeed the thortveitite results are not up to the best current *X*-ray standards). Secondly, in view of the variability of the Si–O–Si angles and of the difference between the P–O–P angles in $P_4O_{10}$ and the third form of $(P_2O_5)_\infty$, study of many more pyrophosphate structures is needed. Thirdly, the results for $Cl_2O_7$ are not up to the standard of the best current electron-diffraction work and they are considerably less accurate than the *X*-ray results for $K_2S_2O_7$. One surprising feature is that the mean Cl–O length in $Cl_2O_7$ is 1·50 Å, which is 0·04 Å larger than in $ClO_4^-$ and 0·025 Å larger than the mean in the simpler perchloric acid studied by the same authors.[68] An accurate re-examination of chlorine heptoxide would be most valuable.

Despite the variation in individual phosphate or silicate structures, there is a definite tendency for the X–O–X angles to get larger as X changes from chlorine to silicon. The most reasonable explanation is that the effect is primarily electrostatic, the forces between adjacent tetrahedra opening the angle beyond 109½°. Such forces will increase as we pass from chlorine to silicon, even though the nominal charges of groups such as $Si_2O_7^{6-}$ are unlikely to be realized. The opening of the angle allows the second π-system to play an increasing part and so reduces the difference between the inner and the outer X–O bonds.

For the final point, we return to the $XO_4$ ions and recall that the observed bond lengths are shorter than the expected single-bond distances by amounts which increase from 0·13 Å in $SiO_4^{4-}$ to 0·22$_5$ Å in $ClO_4^-$. This was interpreted in terms of two π-bonding molecular orbitals, whose group overlaps Jaffé [13] showed to increase markedly from silicon to chlorine owing to the increasing effective nuclear charge for the X(3*d*) orbitals. There is no obvious reason why we should not carry on to the next member of the series, argon tetroxide, and we may therefore predict that, when the difficulties of preparation have been overcome, the neutral molecule $ArO_4$ will be found to have an Ar–O bond of length about 1·45 Å.

(*Note added October 27th*, 1961). Dr. Helen M. Ondik (personal communication) has recently completed structure analyses of the triclinic form of $Na_4P_4O_{12},4H_2O$ and $LiK_2P_3O_9,H_2O$. In the $P_4O_{12}$ ion the average lengths of the two kinds of P–O ring bonds are 1·608 Å and 1·594 Å (±0·005 Å), so that their difference is much smaller than in the two less accurate analyses discussed above. This agrees better with the present theory. In the $P_3O_9$ ion the average bond lengths are 1·61 Å (ring) and 1·48 Å (external), and the average P–O–P angle is 129°.

Results for a structure of type $PO_4R^{2-}$ have been given for calcium thymidylate (Trueblood, Horn, and Luzzati, *Acta Cryst.*, 1961, 14, 965). With approximate rotational

corrections of 0·01 Å, the lengths are P–O(R) = 1·60 Å and P–O = 1·50 Å (±0·01 Å). With the relation of Fig. 20 the predicted lengths are 1·63 and 1·52 Å. The difference between the two lengths is thus about right, but the average P–O length in this structure seems unusually low.

### Appendix

*The Chlorine–Oxygen* 3dπ–2pπ *Overlap Integral.*—No directly relevant self-consistent-field calculations are available, but comparison with s.c.f. wave functions [75] for atoms in the first long row shows that the Slater rules [76] seriously underestimate the effective nuclear charge for 3*d*-orbitals. For instance, in $Ti^+$, with three 3*d*-electrons outside a complete 3*s*,3*p*-shell, the Slater rules give a screening number of $18 + 2 \times 0{\cdot}35 = 18{\cdot}7$ and an effective nuclear charge of $22 - 18{\cdot}7 = 3{\cdot}3$, whereas the s.c.f. calculations correspond to a screening number of 15·6 and an effective nuclear charge of 6·4. This implies that the 3*d*-electrons considerably penetrate the 3*s*,3*p*-shell. As other s.c.f. results suggest a screening number of 0·3 from each other 3*d*-electron, we may roughly take the screening from each 3*s*,3*p*-electron in $Ti^+$ as $(15{\cdot}6 - 10 - 2 \times 0{\cdot}3)/8 = 0{\cdot}625$. In the perchlorate ion this suggests a screening number of $10 + 4 \times 0{\cdot}625 + 2{\cdot}2 \times 0{\cdot}3 = 13{\cdot}16$ for a 3*d*-electron, if the chlorine has a net charge of −0·2 (the precise charge is not important). For an oxygen with a charge of −0·2 the s.c.f. results suggest a screening number of about 4·0. With the appropriate effective nuclear charges of 3·84 and 4·0 and a Cl–O distance of 1·464 Å, Jaffé's tables [77,13] give the overlap integral for 3*d*π with a single 2*p*π as ~0·37, so that the group overlap in the *E* molecular orbital is $\sim 1{\cdot}63 \times 0{\cdot}37 = 0{\cdot}60$. This estimate is obviously rather speculative, but it is supported by Jaffé's calculations with different assumptions.[13]

Department of Inorganic and Structural Chemistry,
The University of Leeds. [*Received, July 3rd*, 1961.]

[75] Hartree, "The Calculation of Atomic Structures," John Wiley, New York, 1957.
[76] Slater, *Phys. Rev.*, 1930, **36**, 57.
[77] Jaffé, *J. Chem. Phys.*, 1953, **21**, 258.

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## 1078. *The Reaction of Metals with* o-*Phenylenebis(diethylphosphine).*

By J. Chatt, F. A. Hart, and D. T. Rosevear.

*o*-Phenylenebisdiethylphosphine reacts with finely divided cobalt, nickel, and palladium at about 200° to form zerovalent complexes of type $[M\{o\text{-}C_6H_4(PEt_2)_2\}_2]$. It does not react with metals neighbouring on these in Group VIII except in the presence of hydrogen. Then it reacts with iron to form a dihydride *trans*-$[FeH_2\{o\text{-}C_6H_4(PEt_2)_2\}_2]$ and with rhodium to form a salt of uncertain structure.

The direct combination of uncharged ligands and metals to form complexes of the metals in their zerovalent states is rare. Until recently the only examples were the combination of carbon monoxide with nickel, iron, and (with difficulty) cobalt, molybdenum, tungsten, rhodium, and ruthenium, to form the metal carbonyls; [1] and of methyldichlorophosphine with metallic nickel to form $[Ni(PMeCl_2)_4]$.[2] The recent discovery [3] that *o*-phenylenebis(diethylphosphine) [4] combines with metallic nickel to form $[Ni\{o\text{-}C_6H_4(PEt_2)_2\}_2]$ has led us to examine its reaction with neighbouring metals in Group VIII.

We have found that the diphosphine dissolves finely divided cobalt and palladium at

[1] Mattern and Gill in "The Chemistry of the Co-ordination Compounds," ed. J. C. Bailar, Jr., Chapman and Hall, Ltd., London 1956, p. 511, and references therein.
[2] Quin, *J. Amer. Chem. Soc.*, 1957, **79**, 3681.
[3] Chatt and Hart, *J.*, 1960, 1378.
[4] Hart, *J.*, 1960, 3324.

about 200° under nitrogen to form complexes of the formula $[M\{o\text{-}C_6H_4(PEt_2)_2\}_2]$ (M = Co or Pd) but does not react with finely divided iron, ruthenium, rhodium, or platinum. Under hydrogen reaction occurs with iron to form a dihydride *trans*-$[FeH_2\{o\text{-}C_6H_4(PEt_2)_2\}_2]$, and with rhodium to form a complex which was obtained in such poor yield that its composition is still uncertain. Cobalt does not form $[CoH\{o\text{-}C_6H_4(PEt_2)_2\}_2]$ under hydrogen but yields the same product as is formed under nitrogen. Neither ruthenium nor platinum reacts under hydrogen

The permanganate-coloured cobalt compound, $[Co\{o\text{-}C_6H_4(PEt_2)_2\}_2]$, is obtained only in poor yield. It sublimes at 160°/0·01 mm. and is so soluble in all organic solvents which do not react with it that it could not be freed entirely from metallic cobalt by recrystallisation. It reacts with hydroxylic solvents and is immediately destroyed by air. We therefore made a more thorough study of the analogous complex $[Co(Ph_2P{\cdot}CH_2{\cdot}CH_2{\cdot}PPh_2)_2]$ which is easier to manipulate and is obtained by reduction of $CoBr_2(Ph_2P{\cdot}CH_2{\cdot}CH_2{\cdot}PPh_2)_2$ with sodium borohydride. This is monomeric in benzene solution, has a magnetic moment of 1·36 B.M., and is isomorphous with the corresponding nickel [3] and palladium [5] complexes.

By analogy with $Ni(CO)_4$ and other 4-co-ordinated $d^{10}$-complexes we should expect these complex compounds of nickel(0) and palladium(0) to have essentially tetrahedral configurations. We therefore presume that the isomorphous cobalt $d^9$ complex has a tetrahedral rather than the alternative planar configuration. Molecular models indicate that a dimeric diamagnetic structure with a Co–Co bond would be very unfavourable sterically. Thus this paramagnetic cobalt(0) complex occupies the same position amongst tetrahedral complexes as do the paramagnetic $[V(CO)_6]$ [6] and $[V(Me_2P{\cdot}CH_2{\cdot}CH_2{\cdot}PMe_2)_3]$ [7] amongst octhedral complexes of zerovalent metals.

The complex $[Pd\{o\text{-}C_6H_4(PEt_2)_2\}_2]$ is the only palladium(0) complex to have been obtained directly from metallic palladium and a ligand. It is formed rather more slowly than the analogous nickel(0) complex [3] and has an almost identical infrared spectrum over the range 4000—450 cm.$^{-1}$. It is a paler orange and is rather less sensitive to air. We presume that it has a tetrahedral configuration.

The dihydridoiron complex *trans*-$[FeH_2\{o\text{-}C_6H_4(PEt_2)_2\}_2]$ was formed in only 7% yield by the direct action of finely divided (pyrophoric) iron on the diphosphine under hydrogen at 200° for 60 hr. In the presence of mercury the yield was increased to 25%. The hydridic proton had a magnetic resonance at $\tau = 23{\cdot}1$. This resonance should be split into five bands by the four equivalent phosphorus nuclei, but only the three strong centre bands were observed. The *trans*-arrangement was confirmed by the low electric dipole moment, which was, however, not measured accurately because in benzene solution the substance is readily oxidised to highly dipolar products. The corresponding dideuteride, prepared under deuterium, was contaminated with hydride because of hydrogen exchange with the ligand. In the infrared spectra $\nu_{Fe\text{-}H}$ occurs at 1726 cm.$^{-1}$, and $\nu_{Fe\text{-}D}$ at 1259 cm.$^{-1}$ in the dihydride and dideuteride, respectively.

The orange-yellow rhodium complex had the composition $Rh_2H_n\{o\text{-}C_6H_4(PEt_2)_2\}_3$, where $n$ is unknown and may be zero because the infrared spectrum gives no evidence of hydridic hydrogen. It was obtained in too small a quantity to establish its exact nature, but it is an electrolyte in acetone solution and has a magnetic moment $\mu_{eff}$ of 1·8 B.M. It may be a complex hydride of general formula, $[RhH_x\{o\text{-}C_6H_4(PEt_2)_2\}_n][RhH_y\{o\text{-}C_6H_4(PEt_2)_2\}_{3-n}]$ ($n \leqslant 3$), related to Farr's " rhodium hydryls." [8]

Preliminary studies show that $Ph_2P{\cdot}CH_2{\cdot}CH_2{\cdot}PPh_2$ has similar power to dissolve metals.

[5] Chatt, Hart, and Watson, unpublished results.
[6] Natta, Ercoli, Calderazzo, Alberola, Corradini, and Allegra, *Atti Accad. naz. Lincei, Rend. Classe Sci. fis. mat. nat.*, 1959, **27**, 107.
[7] Chatt and Watson, *Nature*, 1961, **189**, 1003.
[8] Farr, *J. Inorg. Nucl. Chem.*, 1960, **14**, 202.

## Experimental

In this work a nitrogen-filled glove-box was used. Samples for determination of m. p. were contained in evacuated tubes.

*Di*-o-*phenylenebisdiethylphosphinepalladium*, $[Pd\{o\text{-}C_6H_4(PEt_2)_2\}_2]$.—The diphosphine (1·43 g.) and palladium black (0·90 g.), obtained by magnesium reduction of ammonium chloropalladate(II) in aqueous hydrochloric acid, were heated under nitrogen at 200° for 3 hr. The cooled product was extracted with boiling benzene (25 c.c.), and the cold extract filtered and then evaporated to smaller bulk. Addition of methanol gave orange crystals (0·10 g.) of the *complex*, m. p. 229—230° after two crystallisations from benzene–methanol (Found: C, 54·4; H, 8·0%; *M*, ebullioscopically in 1·17% benzene solution, 564; in 2·09% solution, 632. $C_{28}H_{48}P_4Pd$ requires C, 54·7; H, 7·9%; *M*, 615).

*Di*-o-*phenylenebisdiethylphosphinecobalt*, $[Co\{o\text{-}C_6H_4(PEt_2)_2\}_2]$.—Cobalt (1·66 g.) (obtained by heating cobalt oxalate at 20 mm.) was heated at 200° with the diphosphine (1·23 g.) for 65 hr. The product was extracted with benzene, the extract filtered, and the solvent removed in a stream of nitrogen, leaving a red-black powder (0·16 g.). Sublimation at 160°/0·01 mm. resulted in some decomposition but also gave 0·015 g. of permanganate-coloured *complex* (Found: C, 58·7; H, 8·65. $C_{28}H_{48}CoP_4$ requires C, 59·25; H, 8·6%). The substance is very soluble in most organic solvents, except alcohols, which appear to decompose it, and it is instantly decomposed by air.

*Dibromodi*-1,2-*bisdiphenylphosphinoethanecobalt*, $CoBr_2\{C_2H_4(PPh_2)_2\}_2$.—A solution of cobalt bromide (1·20 g.) in methanol (10 c.c.) was added to a stirred suspension of the diphosphine (3·0 g., 2 mols.) in methanol (50 c.c.). The resulting solution was evaporated to dryness at 12 mm. and the residue, after crystallisation from 3 : 1 ethanol–water (20 c.c.), gave the *complex* as pleochroic black crystals (2·53 g.), decomp. 120—125°, having a green streak (Found: C, 61·9; H, 5·2. $C_{52}H_{48}Br_2CoP_4$ requires C, 61·5; H, 4·8%). This complex ionised in nitrobenzene ($\Lambda_m$ = 14·0 at 26°) to a smaller extent than a uni-univalent electrolyte. Addition of water to its ethanolic solution caused decomposition with precipitation of the diphosphine.

*Di*-1,2-*bisdiphenylphosphinoethanecobalt*, $[Co\{C_2H_4(PPh_2)_2\}_2]$.—A solution of the dibromo-compound described above (1·48 g.) in ethanol (75 c.c.) and water (25 c.c.) was treated with a solution of sodium borohydride (0·166 g., 3 mol.) in water (2 c.c.). The resulting orange precipitate was collected, dried (1·07 g.), and crystallised from benzene–methanol and then from dimethylformamide, giving red crystals of the *complex*, m. p. 280° (decomp.) (Found: C, 72·7; H, 5·9%; *M*, in 1·17% benzene solution, 844; in 1·35% solution, 849. $C_{52}H_{48}CoP_4$ requires C, 73·0; H, 5·65%; *M*, 856). After exposure to hydrogen at 200° for 30 min. the complex showed no evidence of a Co–H stretching band in the infrared spectrum.

*Dihydrodi*-o-*phenylenebisdiethylphosphineiron*, $[FeH_2\{o\text{-}C_6H_4(PEt_2)_2\}_2]$.—Iron powder (1·57 g.) (obtained by heating ferrous oxalate at 20 mm.) was heated with the diphosphine (2·07 g.) and mercury (2 c.c.) under hydrogen at 200° for 88 hr. The product was extracted with benzene, and the extract filtered and evaporated to dryness. Trituration with cold acetone left orange crystals (0·58 g.) which after crystallisation from light petroleum (b. p. 80—100°) gave the pure *product* (0·35 g.), m. p. 248—249·5°; the approximate dipole moment was 1·8 D (Found: C, 59·3; H, 9·0%; *M*, ebullioscopically in 0·753% benzene solution, 557; in 1·879% solution, 565. $C_{28}H_{50}FeP_4$ requires C, 59·4; H, 8·9%; *M*, 566). The dideuteride was prepared similarly, but at 150° to minimise hydrogen–deuterium exchange: the presence of deuterium in the ligand was shown by the infrared spectrum of the product prepared at higher temperatures.

*Action of* o-*Phenylenebisdiethylphosphine on Rhodium*.—The diphosphine (1·91 g.) was heated with rhodium powder (0·91 g.) at 200° for 4 days under hydrogen. The acetone extract, on addition of light petroleum (b. p. 60—80°), gave a product which was redissolved in acetone and reprecipitated with benzene as orange crystals (0·2 g.), m. p. 360–362° (Found: C, 52·35; H, 7·8%). No reaction was observed when rhodium and the diphosphine were heated in an evacuated and sealed tube.

*Action of* o-*Phenylenebisdiethylphosphine on Other Metals*.—The diphosphine (1·0 g.) was heated with (*a*) platinum black (1·3 g.) at 250° for 4½ hr. under carbon dioxide and (*b*) with ruthenium black (0·50 g.) at 200° for 21 hr. under hydrogen. In neither case was a solid product detected.

The dipole moments were determined as described in ref. 9 and the nuclear magnetic resonance and infrared spectra as in ref. 10.

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IMPERIAL CHEMICAL INDUSTRIES LIMITED, HEAVY ORGANIC CHEMICALS DIVISION,
AKERS RESEARCH LABORATORIES, THE FRYTHE,
WELWYN, HERTS. [*Received, August 9th*, 1961.]

[9] Chatt and Shaw, *J.*, 1960, 1718.
[10] Chatt and Hayter, *J.*, 1961, 2605.

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## 1079. *Some Hydrido-complexes of Iron*(II).

By J. CHATT and R. G. HAYTER.

Complexes of the type $[FeCl_2(diphosphine)_2][FeCl_4]$ and $[FeCl_2(diphosphine)_2]$ have been prepared from tertiary diphosphines of the types $C_2H_4(PR_2)_2$ (R = Me or Et) and $o$-$C_6H_4(PEt_2)_2$. From these were prepared monohydrides $[FeHX(diphosphine)_2]$ (X = halogen) and a dihydride $[FeH_2\{o\text{-}C_6H_4(PEt_2)_2\}_2]$ by reduction with lithium aluminium hydride. These have a band in the 1720—1880 cm.$^{-1}$ region due to $\nu_{Fe-H}$, and the Fe-hydrogen atoms show large chemical shifts (up to 39·1 p.p.m.; water standard) in the nuclear magnetic resonance spectrum. The hydrides are oxidised readily in air but show surprising thermal stability, which is attributed to the large ligand field strength of the phosphine ligands and hydride ion.

RECENT communications from these laboratories have reported the preparation of hydrides of the bivalent Group VIII metals Pt, Pd,[1] Fe[2], Ru,[3] and Os,[2,3] which are stabilised by co-ordination to tertiary phosphines and arsines. This paper describes some complexes of ditertiary phosphines with iron halides and their reduction to hydrido-complexes of iron(II). The only previously reported ligand-stabilised mononuclear iron hydrides are the well-known carbonyl hydride, $FeH_2(CO)_4$, and $FeH(CO)_2(C_5H_5)$.[4]

Only a very few complexes of iron(II) or iron(III) with tertiary phosphines or arsines are known,[5] and the types most pertinent to this study are $[FeCl_2\{o\text{-}C_6H_4(AsMe_2)_2\}_2][FeCl_4]$ and $[FeX_2\{o\text{-}C_6H_4(AsMe_2)_2\}_2]$,[6] whose phosphorus analogues we have obtained by reaction between anhydrous ferric or ferrous chloride and the ditertiary phosphines $C_2H_4(PR_2)_2$ (R = Me or Et) and $o$-$C_6H_4(PEt_2)_2$. The ligands $[CH_2]_n(PPh_2)_2$ ($n$ = 1 or 2) also reacted, but the products were not well defined and readily dissociated. The ferric complexes $[FeCl_2(diphosphine)_2][FeCl_4]$ are stable, dark red or green, crystalline, and soluble in polar organic solvents, in which they are ionised, but insoluble in water and hydrocarbons. They react vigorously with lithium aluminium hydride in tetrahydrofuran, with considerable decomposition and precipitation of black solids, probably containing metallic iron. Only the complex $[FeCl_2\{o\text{-}C_6H_4(PEt_2)_2\}][FeCl_4]$ yields a crystalline product, *trans*-$[FeH_2\{o\text{-}C_6H_4(PEt_2)_2\}_2]$, in 5% yield.

The ferrous complexes, *trans*-$[FeCl_2(diphosphine)_2]$, are green, crystalline, and analogous to, although less stable and more reactive than, the corresponding complexes of ruthenium(II) and osmium(II).[7] They are soluble in non-polar solvents and the $C_2H_4(PR_2)_2$

[1] Chatt, Duncanson, and Shaw, *Proc. Chem. Soc.*, 1957, **343**; *Chem. and Ind.*, 1958, 859.
[2] Chatt, Hart, and Hayter, *Nature*, 1960, **187**, 55.
[3] (*a*) Chatt and Hayter, *Proc. Chem. Soc.*, 1959, 153; (*b*) *J.*, 1961, 2605.
[4] Green, Street, and Wilkinson, *Z. Naturforsch.*, 1959, **14b**, 738.
[5] Nyholm, *J. Proc. Roy. Soc. New South Wales*, 1944, **78**, 229; Hieber and Floss, *Z. anorg. Chem.*, 1957, **291**, 314; Naldini, *Gazzetta*, 1960, **90**, 391, 1231.
[6] Nyholm, *J.*, 1950, 851.
[7] Chatt and Hayter, *J.*, 1961, 896.

complex decomposes rapidly in water or alcohol and slowly in moist air. The *trans*-configuration was confirmed by the low dipole moment (1·3 D) of the complex with the diphosphine $C_2H_4(PEt_2)_2$.

*Preparation of Hydrido-complexes.*—The dihydride *trans*-$[FeH_2\{o\text{-}C_6H_4(PEt_2)_2\}_2]$, identical with that formed by the reaction of the diphosphine on finely divided iron under hydrogen,[8] was prepared in 70% yield by reduction of *trans*-$[FeCl_2\{o\text{-}C_6H_4(PEt_2)_2\}_2]$ with lithium aluminium hydride in tetrahydrofuran. Attempts to stop this reaction at the intermediate hydrido-chloride complex were not successful. However, similar reduction of *trans*-$[FeCl_2\{C_2H_4(PR_2)_2\}_2]$ (R = Me or Et) proceeds *via* the red hydridochloride and the reaction can be stopped at this stage by adding ethanol, evaporating the solution, and extracting the product from the solid residue. Further reduction of the hydrido-chlorides derived from the aliphatic diphosphines or isolation without the use of ethanol gave only yellow-orange oils. The infrared spectrum of the product from *trans*-$[FeHCl\{C_2H_4(PEt_2)_2\}_2]$ showed a band at 1817 cm.$^{-1}$, which may be due to the dihydride. *trans*-$[FeHI\{C_2H_4(PEt_2)_2\}_2]$ was made by heating the corresponding hydrido-chloride with sodium iodide in acetone.

*trans*-$[FeHCl\{o\text{-}C_6H_4(PEt_2)_2\}_2]$ was prepared by reaction between *trans*-$[FeH_2\{o\text{-}C_6H_4(PEt_2)_2\}_2]$ and an equivalent of hydrogen chloride in ether. An unidentified white adduct (decomp. 80°) was first precipitated and this, on dissolution in acetone or ethanol, gave the desired hydrido-chloride in about 30% yield. The white product showed no band in its infrared spectrum attributable to $\nu_{Fe-H}$. The properties of the hydrido-complexes are summarised in Table 1.

TABLE 1.

| Compound | M. p.* (in vacuum) | Colour | Dipole moment (D) | $\nu_{Fe-H}$ (Nujol mull) | Chemical shift (p.p.m. $H_2O$ standard), in $C_6H_6$ |
|---|---|---|---|---|---|
| *trans*-$[FeHCl\{C_2H_4(PMe_2)_2\}_2]$ ... | 180° | Red | — | 1810 | — |
| *trans*-$[FeHCl\{C_2H_4(PEt_2)_2\}_2]$ ... | 154·5—155·5 | Red | 4·25 | 1849 | +39·1 |
| *trans*-$[FeHI\{C_2H_4(PEt_2)_2\}_2]$ ... | 173 | Red-brown | — | 1872 | +33·9 |
| *trans*-$[FeHCl\{o\text{-}C_6H_4(PEt_2)_2\}_2]$ | 230·5—231·5 | Red | — | 1870 | +36·0 |

* With decomposition.

The iron hydrides are sensitive to oxidation, especially in solution, and were purified by crystallisation in a nitrogen-filled glove box. They are less stable thermally than the corresponding hydrides of ruthenium(II) and osmium(II).

*Structure.*—The iron hydrido-chlorides show chemical shifts, which are large even for transition-metal hydrides. Each proton resonance of the unique hydrogen atoms consists of five, sharp, equally spaced bands with intensities in the approximate ratios 1 : 4 : 6 : 4 : 1, consistent with coupling between the proton and four equivalent phosphorus nuclei each of spin ½. This pattern confirms the *trans*-structure indicated by dipole-moment measurements. Nuclear resonance and the dipole moments have previously demonstrated *trans*-structures for all the hydrido-tertiary phosphine complexes of platinum, ruthenium, and osmium.

The characteristic infrared frequency due to $\nu_{Fe-H}$ occurs in the range 1810—1872 cm.$^{-1}$ for the hydrido-chlorides and at 1726 cm.$^{-1}$ for the dihydride. The change in frequency with change in ligand and halide anion is in the sense: $C_2H_4(PMe_2)_2 < C_2H_4(PEt_2)_2 < o\text{-}C_6H_4(PEt_2)_2$, and Cl < I, as observed in the ruthenium and osmium series, where this sequence was discussed.[3b] The chemical shifts increase in the reverse direction.

The deuterido-complexes *trans*-$[FeDCl\{C_2H_4(PEt_2)_2\}_2]$ and *trans*-$[FeD_2\{o\text{-}C_6H_4(PEt_2)_2\}_2]$ were prepared by reduction of the corresponding dichloro-complexes with lithium aluminium deuteride in tetrahydrofuran.

[8] Chatt and Hart, unpublished work.

The infrared spectra (Nujol mulls) of the deuterides showed bands due to $\nu_{Fe-D}$ (strong) and $\delta_{Fe-D}$ (weak and broad) shifted by factors of $\sim 2^{-\frac{1}{2}}$ from the corresponding hydrogen vibrations. The results are summarised in Table 2.

TABLE 2.

| | $\nu_{FeH}$ | $\delta_{FeH}$ | $\nu_{FeD}$ | $\delta_{FeD}$ |
|---|---|---|---|---|
| *trans*-$[Fe(H,D)Cl\{C_2H_4(PEt_2)_2\}_2]$ | 1849 | 656 | 1336 | 536 |
| *trans*-$[Fe(H,D)_2\{o\text{-}C_6H_4(PEt_2)_2\}_2]$ | 1726 | 716 | 1259 | 525 |

These hydrides are different in character from the iron carbonyl hydrides where the hydrogen is acidic; *e.g.*, the compound $[FeH_2\{o\text{-}C_6H_4(PEt_2)_2\}_2]$ is unaffected by treatment with metallic lithium in tetrahydrofuran, sodium in liquid ammonia, or dilute aqueous sodium hydroxide.[8] Thus, whereas the carbonyl hydride behaves as if it were polarised in the sense $\overset{\delta-}{Fe}(CO)_4\overset{\delta+}{H_2}$ and the salts $K_2Fe(CO)_4$ were derived from iron(−2), the diphosphine complex behaves more as the first member of a homologous series of iron alkyls derived from iron(II). This behaviour is similar to that of the planar complex phosphino-hydrides, -alkyls, and -aryls of bivalent platinum, palladium, and nickel.[9]

*Thermal Stabilities.*—The thermal stabilities of some complex ruthenium, osmium, and iron hydrides were compared by heating them in pairs in evacuated tubes from room temperature (20°) to their decomposition temperature (*ca.* 300°) at about 4½° per minute (Table 3). Some slight yellowing of the molten compound was sometimes observed before general decomposition with blackening occurred.

TABLE 3.

Vacuum melting and decomposition temperatures of *trans*-$[MXY\{C_2H_4(PEt_2)_2\}_2]$.

| | X = Y = Cl | | X = H, Y = Cl | | X = Y = H | |
|---|---|---|---|---|---|---|
| M | Melts | Decomp. | Melts | Decomp. | Melts | Decomp. |
| Fe | 170° | 170° | 155° | 155° | — | — |
| Ru | 275 | 330 | 175 | 310 | 150° | 280° |
| Os | | | 171 | 315 | 150 | 295 |

It has been proposed that the critical factor in determining the stability of alkyl and aryl compounds of metals with filled or nearly filled non-bonding *d*-orbitals may be the ligand field splitting in the molecule.[9,10] The same argument should apply to these complex hydrides. This would explain why the thermal stability increases as the Group is ascended. The fact that the hydrido-chlorides or dihydrides of ruthenium and osmium are so similar in stability suggests that another factor becomes critical after the necessary ligand field stabilisation has been reached, and that this has been reached in the ruthenium complexes. The only isolated dihydride of iron $[FeH_2\{o\text{-}C_6H_4(PEt_2)_2\}_2]$ decomposes at 248—254° and is more stable thermally than the corresponding halohydride (Table 1). This may also be explained on the above basis since hydrogen in these complexes has a larger ligand splitting than has the halogen.[11] On the other hand, in the ruthenium and osmium complexes where ligand field splitting is not the critical factor, the dihydrides are less stable thermally than the halohydrides.

## EXPERIMENTAL

Microanalyses are by the Microanalytical Department of these Laboratories. M. p.s were in vacuum unless otherwise stated. The hydrides were prepared and handled in a nitrogen-filled glove box. Light petroleum had boiling range 60—80° and molar conductivities were determined in nitrobenzene at 20°.

*Dichlorodi-{o-phenylenebisdiethylphosphine}iron*(III) *tetrachloroferrate*(III) was prepared by

[9] Chatt and Shaw, *J.*, 1960, 1718, and references therein.
[10] Chatt and Shaw, *J.*, 1959, 705.
[11] Chatt and Hayter, *J.*, 1961, 772.

adding the diphosphine (0·475 g., 1·86 mmole) in benzene (10 ml.) to ferric chloride (0·294 g., 1·86 mmole) in ethanol (10 ml.). The dark green precipitate was washed with benzene and crystallised from acetone as black rods (dark green when crushed), m. p. 150—165 (decomp.) (Kofler hot-stage) (66%) [Found: C, 40·2; H, 5·85%; *M* (ebullioscopically in acetone), 426 (0·42% solution), 475 (0·86%). $C_{28}H_{48}Cl_6Fe_2P_4$ requires C, 40·4; H, 5·8%; *M*, 833], molar conductivity 21·5 ohm.$^{-1}$ ($3·2 \times 10^{-3}$M); the nitrobenzene solution was green by transmission and red by reflection. In organic solvents dilute solutions appear to be green, and stronger solutions magenta.

Similarly prepared were:

*Dichlorodi-*{1,2-*bisdiethylphosphinoethane*}*iron*(III) *tetrachloroferrate*(III), from ethanol as dark red needles (85%), m. p. 148·5—149·5° [Found: C, 32·4; H, 6·6%; *M* (ebullioscopically in acetone), 415 (0·45% solution), 421 (0·94%), 437 (1·3%). $C_{20}H_{48}Cl_6Fe_2P_4$ requires C, 32·6; H, 6·6%; *M*, 737], molar conductivity 20·7 ohm$^{-1}$ ($6·6 \times 10^{-3}$M).

*Dichlorodi-*{1,2-*bisdimethylphosphinoethane*}*iron*(III) *tetrachloroferrate*(III), from ethanol as purple-red needles (76%), m. p. 236—236·5° (Found: C, 22·6; H, 5·2. $C_{12}H_{32}Cl_6Fe_2P_4$ requires C, 23·1; H, 5·2%), molar conductivity 22·5 ohm.$^{-1}$ ($3·8 \times 10^{-3}$M).

trans-*Dichlorodi-*{*o-phenylenebisdiethylphosphine*}*iron*(II).—Ferrous chloride tetrahydrate (0·40 g., 2·03 mmole) was dehydrated by azeotropic distillation with benzene during 24 hr. After addition of the diphosphine (1·03 g., 4·1 mmole), ferrous chloride dissolved in a further hour to give a green solution. The solvent was removed at 12 mm. and the residue crystallised from benzene as lime-green rods (60%), m. p. 190—194° (decomp.) (Found: C, 52·7; H, 7·6. $C_{28}H_{48}Cl_2FeP_4$ requires C, 52·9; H, 7·6%).

The following compounds were similarly prepared:

trans-*Dichlorodi-*{1,2-*bisdiethylphosphinoethane*}*iron*(II), from light petroleum as bright green needles (72%), m. p. 168—171·5° (decomp.) (Found: C, 44·3; H, 9·1. $C_{20}H_{48}Cl_2FeP_4$ requires C, 44·55; H, 9·0%).

trans-*Dichlorodi-*{1,2-*bisdimethylphosphinoethane*}*iron*(II), from benzene–light petroleum (1 : 1) as emerald-green prisms (60%), m. p. 255—270° (decomp.), becoming yellow and losing diphosphine (Found: C, 33·7; H, 7·4. $C_{12}H_{32}Cl_2FeP_4$ requires C, 33·75; H, 7·55%).

trans-*Dihydridodi-*{*o-phenylenebisdiethylphosphine*}*iron*(II).—*trans*-Dichlorodi-{*o*-phenylenebisdiethylphosphine}iron(II) (0·50 g.) was suspended in dry tetrahydrofuran (15 ml.) and treated with a solution of lithium aluminium hydride in tetrahydrofuran. The green complex dissolved to give an orange-red solution. When an excess of the hydride was present, the solution was refluxed for 10 min. After cooling, the solvent was removed in a nitrogen stream; the residue, on crystallisation from light petroleum, afforded the pure product in 70% yield as prisms, m. p. 248—254° (decomp.) (Found: C, 59·8; H, 8·9. Calc. for $C_{28}H_{50}FeP_4$: C, 59·4; H, 8·9%). This compound may also be prepared in about 5% yield by similar reduction of $[FeCl_2\{o\text{-}C_6H_4(PEt_2)_2\}_2][FeCl_4]$, and was identified by its infrared spectrum (Nujol mull) and analysis (Found: C, 59·3; H, 8·9%).

trans-*Hydridochlorodi-*{o-*phenylenebisdiethylphosphine*}*iron*(II).—*trans*-Dihydridodi-{*o*-phenylenebisdiethylphosphine}iron(II) (0·15 g.) in benzene (10 ml.) was treated with one equivalent of hydrogen chloride in ether (1·5 ml.) to give a white precipitate (0·16 g.). This product, on being heated in a vacuum, underwent irreversible colour changes to orange (80°), red (150°), black (200°), and melted at 214—218°. It was insoluble in benzene and in light petroleum, but dissolved in boiling acetone or ethanol to give a red solution of the desired product. After refluxing for a few minutes, the solvent was removed and the residue crystallised from light petroleum, yielding the pure *complex* (32%) as needles (Found: C, 55·45; H, 8·1. $C_{28}H_{49}ClFeP_4$ requires C, 56·0; H, 8·2%).

trans-*Hydridochlorodi-*{1,2-*bisdiethylphosphinoethane*}*iron*(II).—*trans*-Dichlorodi-{1,2-bisdiethylphosphinoethane}iron(II) (1·0 g.) in dry tetrahydrofuran (20 ml.) was reduced with lithium aluminium hydride in tetrahydrofuran. An intensely red solution was first obtained, fading to pale yellow when an excess of the reagent was present. Ethanol was then added until effervescence ceased, the red colour being restored. The solvent was removed in a nitrogen stream; the residue, on crystallisation from light petroleum, afforded the pure *product* as needles (83%) [Found: C, 47·1, 48·2; H, 9·6, 9·9; Cl, 6·6, 7·05%; *M* (ebullioscopically in benzene), 526 (0·57% solution), 518 (1·2%), 519 (2·05%). $C_{20}H_{49}ClFeP_4$ requires C, 47·6; H, 9·8; Cl, 7·0%; *M*, 505].

trans-*Hydridochlorodi-*{1,2-*bisdimethylphosphinoethane*}*iron*(II) was analogously prepared as

feathery needles from light petroleum (55% yield) (Found: C, 36·05, 35·9; H, 8·2, 8·3. $C_{12}H_{33}ClFeP_4$ requires C, 36·7; H, 8·5%).

trans-*Hydridoiododi*-{1,2-*bisdiethylphosphinoethane*}*iron*(II).—*trans*-$[FeHCl\{C_2H_4(PEt_2)_2\}_2]$ (0·20 g.) in acetone (10 ml.) was treated with sodium iodide (0·20 g.) in acetone (5 ml.). The solution immediately darkened from red to deep brown and deposited a white precipitate. After being shaken and warmed for 10 min., the solution was filtered and evaporated and the residue crystallised from light petroleum to give the pure *product* as rods (65%) (Found: C, 40·4; H, 8·3; I, 21·5. $C_{20}H_{49}FeIP_4$ requires C, 40·3; H, 8·3; I, 21·3%).

Dipole moments.

| | $10^3\omega$ | $\Delta\varepsilon/\omega$ | $_TP$ | $_EP$ | $_OP$ | $\mu$ |
|---|---|---|---|---|---|---|
| *trans*-$[FeCl_2\{C_2H_4(PEt_2)_2\}_2]$ ..... | 1·388 | 0·882 | | | | |
| | 5·407 | 0·813 | | | | |
| | | | 206 | 150 * | 33 | 1·3 |
| *trans*-$[FeHCl\{C_2H_4(PEt_2)_2\}_2]$ ..... | 9·241 | 4·505 | | | | |
| | 11·65 | 4·468 | | | | |
| | | | 539 | 145 * | 372 | 4·25 |

* Calc. from group refractivities. $-\Delta v/\omega$ was taken as 0·4.

The dipole moments (see Table) were determined as described in ref. 9 and the nuclear magnetic resonance and infrared spectra as in ref. 3*b*.

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[*Received, August 9th*, 1961.]

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## 1080. *The Dielectric Polarization of Some Imperfect Polar Gases.*

By A. D. Buckingham and R. E. Raab.

An apparatus designed to measure the density dependence of the total dielectric polarization of polar vapours is described. Densities and dielectric constants were determined at the same temperature and pressure; pressures up to the saturated vapour pressure at room temperature were also measured. The pressure range of the apparatus is 0—2 atm., at temperatures up to 200°. The expansion of the total polarization $_TP$ as a power series in the density, $_TP = \mathscr{A} + \mathscr{B}/V_m + \ldots$, where $V_m$ is the molar volume, is discussed. Measurements of $\mathscr{A}$ for sulphur hexafluoride, acetonitrile, arsenic trifluoride, fluoroform, and chloroform have been made at several temperatures, leading to dipole moments and polarizabilities. $\mathscr{B}$ has also been found for these polar vapours at a number of temperatures; for acetonitrile at 80°, $\mathscr{B} = -10{\cdot}1 \pm 1{\cdot}1 \times 10^5$ cm.$^6$ mole$^{-2}$, so that at $\frac{1}{3}$ atm. $\mathscr{B}/V_m$ is over 4% of $_TP$. The temperature dependence of $\mathscr{B}$ and of the second virial coefficient $B$ indicates that acetonitrile tends to dimerize, with a heat of dimerization $\Delta H_0 = -3{\cdot}8$ kcal. mole$^{-1}$ and a dimeric dipole moment of 3·4 D; at 100° $-\Delta H_0$ decreases, and the dimer dipole moment increases, as the temperature rises. The dipole moment found for arsenic trifluoride, $2{\cdot}57 \pm 0{\cdot}02$ D, differs interestingly from the microwave Stark-effect value of $2{\cdot}815 \pm 0{\cdot}025$ D. $B$, $\mathscr{A}$, and $\mathscr{B}$ have been measured for arsenic trifluoride, and fluoroform at 80°.

The static dielectric constant $\varepsilon$ of a gas is a potential source of information about the dipole moment $\mu$ and polarizability $\alpha$ of an isolated molecule, and, if measured over a pressure range, about intermolecular forces. The total polarization, or Clausius–Mossotti function, $_TP$ can be expanded as a power series in the gas density [1,2]

$$_TP = \frac{\varepsilon - 1}{\varepsilon + 2} V_m = \mathscr{A} + \mathscr{B}/V_m + \mathscr{C}/V_m^2 + \ldots, \qquad (1)$$

[1] Harris and Alder, *J. Chem. Phys.*, 1953, **21**, 1351.
[2] Buckingham and Pople, *Trans. Faraday Soc.*, 1955, **51**, 1179.

where $V_m$ is the molar volume of the gas, that is, $1/V_m = n$, the number of moles in unit volume; $\mathscr{A}$, $\mathscr{B}$, $\mathscr{C}$, . . ., are the first, second, third, . . ., dielectric virial coefficients, and are functions of the temperature ($T$) [but not of the density, for eqn. (1) is an expansion in powers of this variable]. $\mathscr{A}$ is the dielectric polarization in the limit of zero pressure and is related to the properties of the isolated molecules; it is given by the well-known Debye equation

$$\mathscr{A} = \frac{4\pi N}{3}\left(\alpha + \frac{\mu^2}{3kT}\right) \qquad (2)$$

where $N$ is Avogadro's number and $k$ is Boltzmann's constant. Measurements of ${}_TP$ at low pressures and at several temperatures yield values for $\mu$ and $\alpha$ by way of eqn. (2). Most of the accurately known dipole moments have been found in this way.

$\mathscr{B}$, which is a measure of the initial deviation from ideal-gas behaviour, is related to the properties of an interacting pair of molecules, and it can be shown that for one mole of gas [2]

$$\mathscr{B} = \frac{2\pi N^2}{3\Omega}\int\left\{\alpha_{12} - 2\alpha + \frac{1}{3kT}(\mu_{12}^2 - 2\mu^2)\right\}\exp(-u_{12}/kT)\mathrm{d}\tau_2, \qquad (3)$$

where $\mu_{12}$ and $\alpha_{12}$ are the dipole moment and polarizability of the pair of molecules whose interaction potential energy is $u_{12}$; $\int \mathrm{d}\tau_2 = V_m\Omega$ is an integration over all positions and orientations of molecule 2 ($\int \mathrm{d}\tau_2 = \iiint \mathrm{d}x\mathrm{d}y\mathrm{d}z\int \mathrm{d}\omega = V_m\Omega$, so $\Omega$, a pure number, is the integral over the orientational co-ordinates $\omega$). If $u_{12}$ is such that for the most favourable configuration $-u_{12} \gg kT$, it is helpful to think of a " dimer," that is, a semistable pair of molecules. We then have an equilibrium between monomers X and dimers $X_2$, $2 \rightleftarrows X_2$, and at reasonably low pressures the equilibrium constant $K_c = [X_2]/[X]^2 = -B + O(V_m^{-1})$, where $B$ is the second virial coefficient in the equation of state of the gas: [3,4]

$$pV_m/RT = 1 + B/V_m + C/V_m^2 + \ldots; \qquad (4)$$

$R = Nk$ is the gas constant. In such a case, the dimer is well characterized, $\mathscr{B}$ depending on its polarizability $\langle\alpha_{12}\rangle$ and mean-square dipole moment $\langle\mu_{12}^2\rangle$; these dimeric properties may be temperature dependent, because of the accessibility of low-lying excited vibrational or torsional states.

Thus

$$\mathscr{B} = \frac{4\pi NK_c}{3}\left\langle\alpha_{12} - 2\alpha + \frac{1}{3kT}(\mu_{12}^2 - 2\mu^2)\right\rangle. \qquad (5)$$

For strongly polar monomers, $\alpha_{12} - 2\alpha$ can be neglected, so that

$$\mathscr{B}/\mathscr{A} = K_c\left\{\frac{\langle\mu_{12}^2\rangle}{\mu^2} - 2\right\}. \qquad (6)$$

If the dimer is fairly stable, $\langle\mu_{12}^2\rangle$ will be approximately independent of $T$, and

$$\frac{\mathrm{d}\ln|\mathscr{B}|}{\mathrm{d}T} = \frac{\Delta H_0}{RT^2}, \qquad (7)$$

where $\Delta H_0 = RT^2\dfrac{\mathrm{d}}{\mathrm{d}T}\ln K_p$ is the standard heat of dimerization, $K_p = p_{X_2}/p_X^2$ being the equilibrium constant involving the pressures (in atm.) of the monomer and dimer; $K_p$ is proportional to $K_c/T$ at low pressures. $\mathrm{d}\ln|\mathscr{B}| = \dfrac{1}{\mathscr{B}}\mathrm{d}\mathscr{B}$, so that $|\mathscr{B}|$ is a positive number. If $\Delta H_0$ is approximately independent of $T$, a plot of $\ln|\mathscr{B}|$ against $1/T$ will be linear with slope $-\Delta H_0/R$.

[3] Beattie and Stockmayer, in Taylor and Glasstone, " Treatise on Physical Chemistry," Macmillan, London, 1951, Vol. II, chap. 2.

[4] Buckingham and Raab, *Trans. Faraday Soc.*, 1959, **55**, 377.

If both monomer and dimer are non-polar, as would be the case for the equilibria

$$2I \rightleftharpoons I_2 \text{ and } 2Al(CH_3)_3 \rightleftharpoons Al_2(CH_3)_6$$

(assuming the monomeric trimethylaluminium to be planar), the polarizability term in (5) is dominant, and

$$\mathscr{B}/\mathscr{A} = K_c\left\{\frac{\langle\alpha_{12}\rangle}{\alpha} - 2\right\}, \quad \frac{\mathrm{d}\ln|\mathscr{B}|}{\mathrm{d}T} = \frac{\Delta H_0}{RT^2} + \frac{1}{T}; \qquad (8)$$

$\Delta H_0/RT$ may be of the order $-10$ at room temperature, so that eqn. (7) indicates that $|\mathscr{B}|$ may decrease by a few units % for each degree rise in temperature.

Measurements of ${}_TP$, leading to values for $\mathscr{A}$ and $\mathscr{B}$, have been reported for a number of polar and non-polar gases; results are summarized in Table 1. It is clear that $\mathscr{B}$ can be of either sign, and varies considerably from one substance to another. For the inert gases, $\mu$ and $\mu_{12}$ are zero (but $\mu_{123} \neq 0$), and $\mathscr{B}$ arises purely from the effects of the interaction on the polarizability; for the non-dipolar gases methane, nitrogen, carbon dioxide, and ethane, although $\mu = 0$, $\mu_{12} \neq 0$, and a substantial contribution to $\mathscr{B}$ arises from the dipole moment induced in a molecule by the quadrupole or octopole moment of its neighbour.[5,10] Much larger values of $\mathscr{B}$ are found for highly polar gases, and the non-polar contributions may be neglected. The sign of $\mathscr{B}$ has been interpreted [2] in terms of a " shape " effect, rod-like polar molecules (methyl fluoride being a not very good example of this class) having a tendency towards an antiparallel alignment, leading to a small $\mu_{12}$ and hence to a negative $\mathscr{B}$, while disc-shaped molecules such as ammonia tend to form pairs with parallel dipoles, producing a positive $\mathscr{B}$.

All the substances in Table 1 are permanent gases, and the measurements of $\varepsilon$ and $p$

TABLE 1.

Previous values of dielectric virial coefficients.

| Substance | Temp. | $\mathscr{A}$(cm.$^3$ mole$^{-1}$) | $\mathscr{B}$(cm.$^6$ mole$^{-2}$) | Ref. |
|---|---|---|---|---|
| He | 23° | 0·522 | −0·5 | 5 |
| Ar | −31 | 4·14 | 0·6 | 5 |
| Ar | 33 | 4·14 | 1·0 | 5 |
| $N_2$ | −31 | 4·39 | 4·2 | 5 |
| $N_2$ | 71 | 4·39 | 0·0 | 5 |
| $CH_4$ | −31 | 6·52 | 9·0 | 5 |
| $CO_2$ | 22 | 7·35 | 64 ± 10 | 6 |
| $C_2H_4$ | 50 | 10·69 | 25 ± 7 | 7 |
| $NH_3$ | 100 | 41·35 | 440 | 8 |
| $CH_3F$ | 50 | 70 | −600 | 9 |

were made up to quite high pressures (~100 atm.). At lower reduced temperatures, $|\mathscr{B}|$ will presumably be larger, but the maximum attainable pressures will be smaller. This paper reports new measurements of ${}_TP$ for some highly polar vapours in the pressure range 0—2 atm.

## EXPERIMENTAL

To measure ${}_TP$, both $\varepsilon$ and $V_m$ must be determined. $\varepsilon$ has frequently been obtained, as in this investigation, by determining the change in capacity of a condenser when a gas is admitted to it, a precision variable condenser being used to keep the total capacity constant.

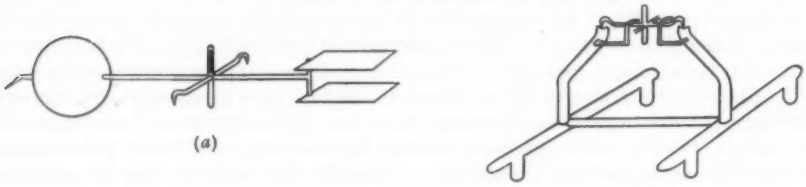
[5] Johnston, Oudemans, and Cole, *J. Chem. Phys.*, 1960, **33**, 1310.
[6] Michels and Kleerekoper, *Physica*, 1939, **6**, 586; de Wijn and Heineken, *Physica*, 1959, **25**, 615.
[7] David, Hamann, and Pearse, *J. Chem. Phys.*, 1951, **19**, 1491.
[8] Keyes and Kirkwood, *Phys. Rev.*, 1930, **36**, 1570.
[9] David, Hamann, and Pearse, *J. Chem. Phys.*, 1952, **20**, 969.
[10] Buckingham and Pople, *Trans. Faraday Soc.*, 1955, **51**, 1029.

In earlier work, $V_m$ was found through $p$ (and $T$), and the ideal-gas equation $pV_m = \boldsymbol{RT}$, or, when imperfections were being studied, eqn. (4). From eqns. (1) and (4) we have

$$\frac{\varepsilon - 1}{\varepsilon + 2} \cdot \frac{\boldsymbol{RT}}{p} = \mathscr{A} + \frac{p}{\boldsymbol{RT}}(\mathscr{B} - \mathscr{A}B) + O(p^2), \qquad (9)$$

and the initial slope of the experimental quantity $\frac{\varepsilon - 1}{\varepsilon + 2} \cdot \frac{\boldsymbol{RT}}{p}$ as a function of $p/\boldsymbol{RT}$ is $\mathscr{B} - \mathscr{A}B$, while the desired quantity is $\mathscr{B}$. For methyl fluoride at 50°, $\mathscr{B}/\mathscr{A} = -8$ cm.$^3$ mole$^{-1}$, while $B = -171$ cm.$^3$ mole$^{-1}$.[11] To determine $\mathscr{B}$ by that means to an accuracy of 10%, $B$ must be known to better than 0·5%; an uncertainty of 0·1° in the temperature at which $\varepsilon$ is measured would lead to an error of 10% in $\mathscr{B}$. These difficulties are avoided in the present experiments by using a precision gas-density balance alongside the gas condenser, so $\varepsilon$ and $V_m$ are determined directly at the same temperature.

FIG. 1. The gas density balance and its support.



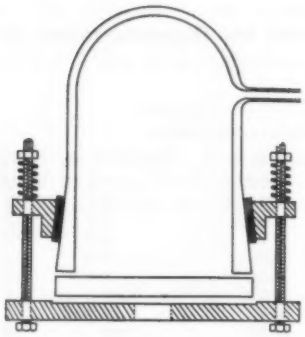



FIG. 2. The density-balance container.

Unhatched = glass,
Wide hatching = steel,
Close hatching = asbestos.

*The Density Balance.*—As a null instrument, the gas-density balance has been successfully used for measurements of high precision; sensitivity to a change smaller than that detectable with a mercury manometer has been claimed for the most refined balances.[12,13] The balance described below measured densities from 0 to 0·01 g. cm.$^{-3}$ with an accuracy of better than 0·1% at the highest densities. It is shown, with its glass support, in Fig. 1. The movable parts were made from silica, and inaccuracies arising from adsorption were minimized by making the moment of the surface area of the plates equal to that of the bulb. The restoring torque was supplied by the extra weight of the solid central rod below the pivots relative to that of the hollow one above. The pivots were two silica points, supported by hemispherical cups; two small arms prevented the balance points being thrown out of the cups. The overall length of the beam was 13·5 cm., and the bulb diameter 3·1 cm. The period of a swing was 3·0 sec., and the plates were horizontal to assist damping. In a vacuum, the beam was at 27° below the horizontal and it could rise to 45° above it, yielding a full-scale vertical pointer movement of 10 cm. The pointer's position was measured with a cathetometer reading to 0·001 cm. A reading was made by determining the pressure of a standard gas (carbon dioxide or sulphur

[11] Hamann and Pearse, *Trans. Faraday Soc.*, 1952, **48**, 101.
[12] Whytlaw-Gray, *Quart. Rev.*, 1950, **4**, 153.
[13] Lambert and Phillips, *Phil. Trans.*, 1950, *A*, **242**, 415.

hexafluoride) required to produce the same deflection; this was always done immediately after an observation on an unknown value, thereby eliminating errors arising from temperature fluctuations or from a movement of the balance points in their supporting cups.

*The Density-balance Container.*—The housing for the density balance was made from "Pyrex Pipeline" of 4 in. internal diameter and a Pyrex optical window $\frac{1}{4}$ in. thick. A $\frac{1}{8}$ in. gasket-ring of polytetrafluoroethylene separated the two, and was squeezed by six spring-loaded bolts passing through a steel backing-plate. The container withstood the pressure of 3 atm. of air inside it at temperatures up to 250° without significant leakage. The backing-plate had a rectangular slit through which the balance pointer was observed.

*The Gas Cell.*—This has already been described.[14] It consisted of three coaxial platinum cylinders, the inner- and the outer-most one being earthed, all mounted inside a glass tube through which tungsten leads passed. The capacity of the evacuated cell at room temperature was 142 μμF.

*The Precision Condenser.*—This was of the stepped-rod type used by Le Fèvre *et al.*[15] in studies of gas dipole moments. The rod and cylinder were of stainless steel and were accurately machined so that their surfaces had no humps higher than 0·0001 in. and their diameters were constant to 0·0005 in. The rod was pushed (not turned) by a micrometer screw, contact being made through a steel ball to reduce friction. The rod was kept in contact with the micrometer by the tension in a Nylon wire supporting a weight over a pulley. The two bearings were of brass and were V-shaped. The live cylinder through which the rod moves was contained within an earthed cylindrical shield fixed to the steel base plate of the condenser. The live cylinder was supported at both ends by three glass rods mounted in brass screws threaded in the earthed outer cylinder. The glass rods fitted into small countersunk holes symmetrically cut in the outer surface of the live cylinder, whose position could easily be adjusted with the screws; the linear dependence of the capacity change on the micrometer setting was established by using the heterodyne beat oscillator (see below). End-effects were reduced by guard rings at both ends of the earthed shield. The lead from the live cylinder passed through a glass bush mounted on the earthed tube, and the rod and cylinders were enclosed in a Perspex dust cover.

The micrometer had a 5 cm. movement produced by 100 turns of the drum which had 250 divisions; each drum division could be subdivided by eye to $\frac{1}{4}$ division. The stepped-rod had a diameter of 0·6854 in. for 5·3 in., and 0·4354 in. for 6·2 in., and the live cylinder had an internal diameter of 1·0039 in. and was 7 in. long. The base-plate was 17 × 4 × 0·7 in., so the whole condenser was large and heavy. The dimensions were calculated to give a full-scale capacity change of 4 μμF, easily readable on the micrometer to $10^{-4}$ μμF.

*The Oscillators and Detectors.*—The capacity change $\Delta C$ arising from the admission of a vapour to the gas cell was measured by incorporating the precision variable condenser in parallel with the gas cell into an LC oscillator. This transitron oscillator was similar to that described by Hill,[14] but incorporated a number of modifications aimed at improving the frequency stability. The circuits of the oscillator and its buffer (whose purpose is to overcome any tendency the variable oscillator may have to be "pulled" by the fixed-frequency reference oscillator when their frequency difference is small) are shown in Fig. 3. The valve filaments were supplied from a large 6-v accumulator, and the high tension from a Solartron type AS 517 unit giving a very stable 250 v source, which was used (with a thermally insulated resistor) to provide both the required high voltages.

As described by Hill,[14] the oscillator was compared with an identical unit supplied from the same voltage sources, and the frequency difference determined by beating it against a fixed audio-oscillator, the Lissajou figures being observed on an oscilloscope. By returning to the same figure, it was possible to tune the variable oscillator to the same frequency. However, the accuracy of this method depended on the stability of the reference radio- and audio-frequencies. It was used for the calibration and alignment of the precision variable condenser, for by observing the movement of the micrometer required to reproduce a given Lissajou figure, the change in setting $\Delta l$ for a fixed capacity change $\Delta C$ could be determined over different parts of the micrometer scale. For the determination of $\epsilon$, a more accurate approach was used, involving direct comparison of the frequency of the variable oscillator with that of a harmonic oscillator (Fig. 4), whose frequency was locked by a 100 kc. sec.$^{-1}$ signal (stable to 1 part in $10^8$) from a thermostat-controlled crystal; the harmonic at 500 kc. sec.$^{-1}$ was selected and used as

[14] Coop and Sutton, *J.*, 1938, 1269; R. A. W. Hill, D.Phil. Thesis, Oxford, 1949.
[15] Le Fèvre, Ross, and Smythe, *J.*, 1950, 276.

the reference. This beat directly against the variable oscillator, and a microammeter served as a detector. At zero beat, the ammeter needle was stationary, and for a beat of 1 cycle sec.$^{-1}$ it made one oscillation per sec. This was highly sensitive, and frequency differences of 0·02 cycle sec.$^{-1}$ could be detected; no tendency to " pull " the variable oscillator was noticed, even at frequency differences as small as 0·02 cycle sec.$^{-1}$, so the buffer in Fig. 4, with a transformer ratio of 100 : 1, was satisfactory. The beat-detector circuit is shown in Fig. 5. The oscillators

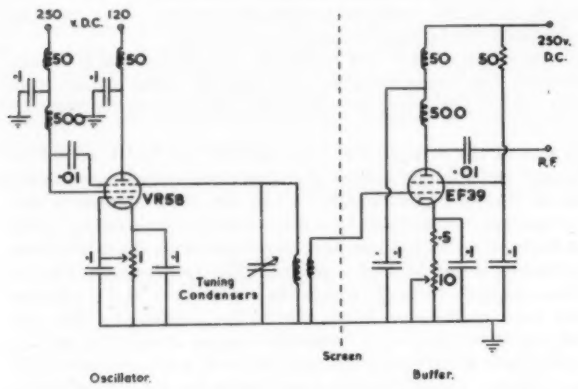



FIG. 3. Radio-frequency oscillator and buffer.
Units: R in KΩ; C in μF; L in mH.

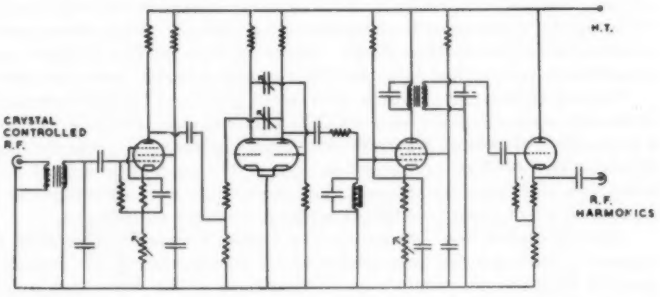



FIG. 4. The crystal-controlled harmonic oscillator.

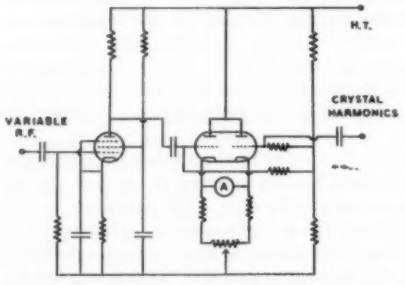



FIG 5. The zero-beat detector.

and the precision condenser were housed in a large, thermally insulated and electrically screened box; the micrometer was turned by a shaft connected to a geared wheel outside the box, and read through a double window in the top of the box. The frequency drift of the variable oscillator was rarely worse than $\frac{1}{4}$ cycle sec.$^{-1}$ in 5 min.

*The Constant-temperature Vapour Bath.*—The problem of producing constant temperatures up to 250° was solved by using a vapour bath, containing a double window of optical glass through which the density-balance pointer could be seen. The gas cell and the density balance were placed at approximately symmetrical positions inside the bath. The boiler, which was

detachable from the bath, was electrically heated, and the vapour condensed at the top and returned to the bottom of the bath. The lid, window, and boiler were attached to the brass bath by steel bolts with asbestos–graphite gaskets, and as the temperature rose there was a tightening, so that vapour leaks were not troublesome. The glass leads were taken through the lid with polytetrafluoroethylene washers, and the whole bath (except the window) was well lagged on its outer surface. The liquids used were benzene (80°), methylcyclohexane (100°), chlorobenzene (131°), and cyclohexanol (160°).

*The Gas Line.*—Pumping was by a mercury diffusion pump backed by a rotary pump. Substances were introduced into traps by condensation with liquid air. Polar liquids were then distilled, through $P_2O_5$, first and last fractions being rejected. The standard gases (carbon dioxide and sulphur hexafluoride) were purified by subliming them several times over $P_2O_5$. The gas line to the vapour bath could be heated by nichrome wire fed by a variable voltage. Taps subjected to pressures above 1 atm. were spring-loaded, and the high temperature taps lubricated with " Kel-F " grease.

The manometer tube had a bore of 13 mm., and one limb was either evacuated or opened to the atmosphere for pressure measurements from 1 to 2¼ atm. The mercury level was observed through a microscope attached to a 1 m. cathetometer reading to 0·001 cm.

*Procedure.*—After the temperature inside the vapour bath had become steady, the vacuum reading of the precision condenser was recorded. Vapour was then admitted to the apparatus and as soon as equilibrium had been reached (that is, after a few minutes) the precision condenser was adjusted to give a zero beat frequency on the microammeter detector, and the density balance position was noted. The apparatus was then slowly evacuated and the precision condenser reading again found. Next, standard gas was sublimed slowly into the apparatus to give a density slightly greater than that of the vapour. The balance pointer was allowed to come to rest and the density then adjusted, by means of a capillary, until the pointer returned to its original position. The pressure of the standard gas was noted. The precision condenser was read before and immediately after evacuation of the standard to give a calibration point.

*Errors.*—Pressures are quoted in cm. Hg at 0°, and are accurate to 0·002 cm. Small corrections were applied because of the meniscus [16] and the thermal expansion of mercury and the brass cathetometer scale.

The temperature of the vapour bath was observed for each measurement of $\varepsilon$ and $V_m$. Four mercury-in-glass thermometers were used to cover the range 80—160°; they were immersed to a definite depth in the bath, and had been compared with thermometers calibrated by the National Physical Laboratory. The maximum error is probably 0·05°. Adjustments to the final $_TP$ values were made when the temperature changed slightly during a run.

The density of the unknown vapour is equal to that of the standard gas for the same deflection of the density balance, so the molar volume $V_X$ of a substance of molecular weight $M_X$ is related to that of the standard (subscript s) by [see eqn. (4)]

$$V_X = \frac{M_X}{M_s} \cdot V_s = \frac{M_X}{M_s}\left\{\frac{RT}{p_s} + B_s + O(p_s)\right\}. \qquad (10)$$

The required values of $B_s$ for carbon dioxide and sulphur hexafluoride were obtained from the data of MacCormack and Schneider.[17] The reproducibility of the setting of the density balance was found to be unsatisfactory below about $3 \times 10^{-4}$ g. cm.$^{-3}$ (0·2 atm. of carbon dioxide), but at higher densities the setting was accurate within 0·1%, provided the balance was not subjected to shock. (The need for care in avoiding mechanical shock and sudden draughts might be overcome by replacing the point-and-cup supports by a horizontal quartz fibre suspension; this would also render the restoring rods unnecessary.)

The main cause of error in the dielectric constant is frequency drift in the variable oscillator. This is normally stable to better than ¼ cycle sec.$^{-1}$ in the time required for two successive condenser readings. For an operating frequency of 500 kc. sec.$^{-1}$ and when half the total capacity of the oscillator is supplied by the gas cell, this drift leads to an error of $2 \times 10^{-6}$ in $(\varepsilon - 1)$. For 1·4 atm. of carbon dioxide, or 0·04 atm. of acetonitrile, at 100°, $(\varepsilon - 1) = 1000 \times 10^{-6}$, and this corresponds to approximately three turns of the micrometer drum;

[16] Cawood and Patterson, *Trans. Faraday Soc.*, 1933, **29**, 514.
[17] MacCormack and Schneider, *J. Chem. Phys.*, 1950, **18**, 1269; 1951, **19**, 845.

thus the effect of the error in reading the micrometer is small compared with that of the frequency drift. At each temperature, a "calibration constant," $f$, was obtained (by using carbon dioxide or sulphur hexafluoride), where $\varepsilon - 1 = f\Delta l$, $\Delta l$ being the movement (in cm.) of the precision condenser. It has been found that $f = 5{\cdot}5514 \times 10^{-3}(1 - 48{\cdot}83 \times 10^{-6}t)$ cm.$^{-1}$, where $t$ is the temperature in °c. The uncertainty in $f$ is about 0·1% at the highest temperatures, and considerably less at lower temperatures.

At the highest densities, the absolute error in ${}_TP$ is of the order of 0·2% (half of which is due to uncertainties in the density and half to the error in $f$), but at lower densities it is larger. However, the relative errors important for the determination of $\mathscr{B}$ are about half of these, and arise chiefly from the uncertainty in $V_m$. At very low densities, direct measurement of the pressure of the vapour becomes possible and at pressures of about 5 cm. Hg the error in ${}_TP$ for acetonitrile is only about 0·1%.

For calibration, it was assumed that $\mathscr{A}$ for carbon dioxide is 7·35 cm.$^3$ mole$^{-1}$,[18] and all our measured values of ${}_TP$ are proportional to this number. We have found that for sulphur hexafluoride $\mathscr{A} = 16{\cdot}41 \pm 0{\cdot}02$ cm.$^3$ mole$^{-1}$.

*Materials.*—Substances were purified immediately before use, as indicated above, and rejected immediately afterwards.

Sulphur hexafluoride, supplied in a cylinder by Imperial Chemical Industries Limited, contained $H_2O < 1$, $SF_4 < 4$, and $S_2F_{10} < 1$ p.p.m.

Acetonitrile, supplied by B.D.H., was dried ($CaCl_2$, then KOH) and distilled; a middle fraction of b. p. 81·1°/75 cm. was collected.

Arsenic trifluoride was prepared by warming a mixture of calcium fluoride and arsenic trioxide with concentrated sulphuric acid. It was distilled in dry nitrogen and stored over sodium fluoride. A middle fraction of b. p. 57·7°/77 cm. was collected.

Fluoroform was obtained from Imperial Chemical Industries Limited as "Arcton 1."

Chloroform, supplied by B.D.H., was distilled over $P_2O_5$, a fraction boiling at 61·1°/75·4 cm. being collected.

## Results and Discussion

(a) *Sulphur Hexafluoride.*—The values of $\mathscr{A}$ in Table 2 are independent of temperature, confirming the non-polarity of sulphur hexafluoride; alternatively, the constancy of

Table 2.

Measurements on $SF_6$.

| Temp. | $p$ (cm. Hg) | $10^6(\varepsilon - 1)$ | ${}_TP$ (cm.$^3$ mole$^{-1}$) | $\mathscr{A}$ (cm.$^3$ mole$^{-1}$) |
|---|---|---|---|---|
| 80·69° | 87·255 | 1962·9 | 16·42 | 16·42 ± 0·01 |
| ($B = -182$ cm.$^3$ mole$^{-1}$) | 90·521 | 2034·2 | 16·39 | |
| | 75·937 | 1711·3 | 16·46 | |
| | 75·255 | 1691·9 | 16·42 | |
| | 75·834 | 1703·5 | 16·41 | |
| | 76·631 | 1723·1 | 16·42 | |
| 100·35° | 71·518 | 1518·0 | 16·39 | 16·41 ± 0·01 |
| ($B = -162$) | 79·431 | 1692·4 | 16·44 | |
| | 79·057 | 1681·1 | 16·41 | |
| | 76·186 | 1618·0 | 16·40 | |
| | 75·884 | 1611·1 | 16·39 | |
| | 73·801 | 1573·7 | 16·46 | |
| | 74·381 | 1580·0 | 16·40 | |
| | 75·515 | 1606·4 | 16·42 | |
| 131·78° | 86·369 | 1693·0 | 16·42 | 16·41 ± 0·004 |
| ($B = -134$) | 82·436 | 1615·1 | 16·41 | |
| | 82·998 | 1626·4 | 16·41 | |
| | 82·401 | 1614·3 | 16·41 | |
| | 81·203 | 1590·1 | 16·40 | |
| | 84·370 | 1653·1 | 16·41 | |

The errors quoted are standard deviations from the mean, calculated by the method of least squares. No attempt was made to determine $\mathscr{B}$.

[18] Maryott and Buckley, "Table of Dielectric Constants and Electric Dipole Moments of Substances in the Gaseous State," Nat. Bureau Standards, Washington, 1953, Circular 537.

$\mathscr{A}$ can be considered as a check on the carbon dioxide calibration. Previous values of $\mathscr{A}$ for this fluoride are 16·5, 16·8, and 15·7 cm.$^3$ mole$^{-1}$,[18] in agreement with our mean value of 16·41 ± 0·02 cm.$^3$ mole$^{-1}$ (relative to $\mathscr{A}_{CO_2} = 7{\cdot}35$), where the stated error includes that arising from the calibration of the condenser. Sulphur hexafluoride, which is easy to purify and to handle, with its large polarizability, might prove to be a better standard than carbon dioxide for future gas dielectric constant measurements.

(b) *Acetonitrile.*—The saturated vapour pressure of this substance at room temperature (0·1 atm.) is sufficiently high to enable accurate values of $_TP$ to be obtained by direct measurement of $p$ with the manometer, in the low-pressure region where the density balance is insensitive. The values of $V_m^{-1}$ less than $0{\cdot}3 \times 10^{-5}$ cm.$^{-3}$ were obtained by measurements of $p$ and the use of the second virial coefficients [19] listed in the first column of Table 3. Fig. 6 illustrates the dependence of $_TP$ on $1/V_m$ at four temperatures.

" Least squares " fitting of the values of $_TP$ to curves of the type of eqn. (1) (stopping

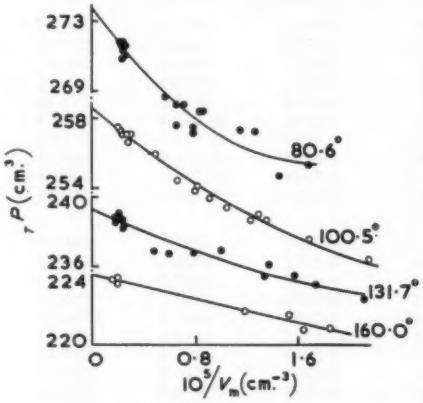



FIG. 6. The temperature and density dependence of the total polarization of $CH_3{\cdot}CN$.

at the third dielectric virial coefficient for $T = 81°$, 100°, and 132°, and at the second for the highest temperature) lead to the following results:

$T = 80{\cdot}64°$, $_TP = 273{\cdot}68 - 10{\cdot}13 \times 10^5 V_m^{-1} + 2{\cdot}92 \times 10^{10} V_m^{-2}$, $\mathscr{A} = 273{\cdot}68 \pm 0{\cdot}33$ cm.$^3$ mole$^{-1}$, $\mathscr{B} = -10{\cdot}1 \pm 1{\cdot}1 \times 10^5$ cm.$^6$ mole$^{-2}$.

$T = 100{\cdot}48°$, $_TP = 258{\cdot}50 - 6{\cdot}132 \times 10^5 V_m^{-1} + 0{\cdot}955 \times 10^{10} V_m^{-2}$, $\mathscr{A} = 258{\cdot}50 \pm 0{\cdot}17$ cm.$^3$ mole$^{-1}$, $\mathscr{B} = -6{\cdot}13 \pm 0{\cdot}34 \times 10^5$ cm.$^6$ mole$^{-2}$.

$T = 131{\cdot}69°$, $_TP = 239{\cdot}26 - 3{\cdot}43 \times 10^5 V_m^{-1} + 0{\cdot}54 \times 10^{10} V_m^{-2}$, $\mathscr{A} = 239{\cdot}26 \pm 0{\cdot}15$ cm.$^3$ mole$^{-1}$, $\mathscr{B} = -3{\cdot}43 \pm 0{\cdot}58 \times 10^5$ cm.$^6$ mole$^{-2}$.

$T = 160{\cdot}00°$, $_TP = 224{\cdot}01 - 1{\cdot}718 \times 10^5 V_m^{-1}$, $\mathscr{A} = 224{\cdot}01 \pm 0{\cdot}11$ cm.$^3$ mole$^{-1}$, $\mathscr{B} = -1{\cdot}72 \pm 0{\cdot}11$ cm.$^6$ mole$^2$.

Fitting the four values of $\mathscr{A}$ to eqn. (2) leads to $\mathscr{A} = 3{\cdot}304 + 95{,}550/T$, whence $\alpha = 1{\cdot}3 \pm 0{\cdot}5 \times 10^{-24}$ cm.$^3$, $\mu = 3{\cdot}96 \pm 0{\cdot}01$D. The molar refraction $[R]_D$ for the sodium D line is [18] 11·1 cm.$^3$, so there is little doubt that our $\alpha$ is too small. Because of the large extrapolation to infinite temperature, the error in $\alpha$ is large, and a small error in the carbon dioxide calibration would seriously affect $\alpha$ (but not $\mu$). The dipole moment agrees well with the 3·96 D of Groves and Sugden [20,18] and the 3·92 ± 0·06 D obtained through Stark-effect measurements.[21] If the distortion polarization, $_DP$, is equal to

[19] Lambert, Roberts, Rowlinson, and Wilkinson, *Proc. Roy. Soc.*, 1949, *A*, **196**, 113; McGlashan, " Tables of Second and Third Virial Coefficients of Gases," University of Reading, 1955.
[20] Groves and Sugden, *J.*, 1937, 158.
[21] Ghosh, Trambarulo, and Gordy, *J. Chem. Phys.*, 1953, **21**, 308; *Phys. Rev.*, 1952, **87**, 172.

TABLE 3.

Measurements on $CH_2{\cdot}CN$.

| Temp. | $10^5 V_m^{-1}$ (cm.$^{-3}$) | $10^6(\varepsilon - 1)$ | $_TP$ (cm.$^3$ mole$^{-1}$) | $10^5 V_m^{-1}$ (cm.$^{-3}$) | $10^6(\varepsilon - 1)$ | $_TP$ (cm.$^3$ mole$^{-1}$) |
|---|---|---|---|---|---|---|
| 80·64° | 0·2196 | 1791·7 | 271·84 | 0·2696 | 2193·6 | 271·04 |
| ($B = -2420$ | 0·2338 | 1906·1 | 271·62 | 0·5670 | 4576·6 | 268·66 |
| cm.$^3$ mole$^{-1}$) | 0·2338 | 1907·8 | 271·85 | 0·6520 | 5256·0 | 268·24 |
| | 0·2384 | 1938·4 | 270·85 | 0·6575 | 5277·2 | 267·06 |
| | 0·2385 | 1946·5 | 271·82 | 0·7053 | 5685·2 | 268·20 |
| | 0·2397 | 1952·3 | 271·27 | 0·7868 | 6306·9 | 266·64 |
| | 0·2407 | 1960·3 | 271·34 | 0·7868 | 6313·6 | 266·91 |
| | 0·2463 | 2009·8 | 271·82 | 0·8381 | 6748·4 | 267·81 |
| | 0·2520 | 2049·7 | 270·94 | 0·8608 | 6933·2 | 267·85 |
| | 0·2537 | 2065·7 | 271·26 | 1·1447 | 9188·7 | 266·75 |
| | 0·2564 | 2086·2 | 271·30 | 1·2603 | 10,116·3 | 266·66 |
| | 0·2567 | 2090·2 | 271·21 | 1·4505 | 11,538·6 | 264·16 |
| | 0·2681 | 2185·9 | 271·57 | 1·6759 | 13,371·6 | 264·78 |
| 100·48° | 0·2056 | 1588·6 | 257·44 | 0·8146 | 6221·6 | 254·07 |
| ($B = -1880$) | 0·2225 | 1718·4 | 257·23 | 0·9079 | 6918·4 | 253·42 |
| | 0·2365 | 1824·8 | 257·02 | 1·0471 | 7964·7 | 252·87 |
| | 0·2661 | 2053·3 | 257·01 | 1·2289 | 9325·2 | 252·15 |
| | 0·2695 | 2079·5 | 257·06 | 1·2914 | 9813·2 | 252·48 |
| | 0·2805 | 2161·3 | 256·63 | 1·3522 | 10,262·4 | 252·13 |
| | 0·2805 | 2164·3 | 256·98 | 1·6824 | 12,724·5 | 251·05 |
| | 0·3030 | 2338·6 | 257·08 | 2·1463 | 16,177·4 | 249·90 |
| | 0·4883 | 3753·6 | 255·91 | 2·3228 | 17,529·5 | 250·09 |
| | 0·6648 | 5082·0 | 254·40 | 2·7930 | 20,946·5 | 248·26 |
| | 0·7985 | 6092·6 | 253·82 | | | |
| 131·69° | 0·1785 | 1279·2 | 238·76 | 0·2464 | 1761·8 | 238·25 |
| ($B = -1410$) | 0·1832 | 1311·2 | 238·50 | 0·2511 | 1796·6 | 238·32 |
| | 0·1870 | 1338·5 | 238·49 | 0·4747 | 3377·3 | 236·86 |
| | 0·1942 | 1391·4 | 238·71 | 0·5895 | 4192·4 | 236·70 |
| | 0·2129 | 1527·1 | 238·03 | 0·7822 | 5565·3 | 236·73 |
| | 0·2172 | 1556·4 | 238·69 | 0·9995 | 7119·4 | 236·88 |
| | 0·2190 | 1569·4 | 238·80 | 1·3399 | 9494·4 | 235·46 |
| | 0·2299 | 1648·3 | 238·85 | 1·3708 | 9740·9 | 236·09 |
| | 0·2339 | 1674·7 | 238·56 | 1·5624 | 11,078·3 | 235·44 |
| | 0·2343 | 1677·3 | 238·54 | 1·7310 | 12,251·0 | 234·95 |
| | 0·2403 | 1721·8 | 238·68 | 2·1053 | 14,865·3 | 234·14 |
| | 0·2438 | 1743·1 | 238·22 | | | |
| 160·00° | 0·1550 | 1040·6 | 223·72 | 1·1802 | 7877·8 | 221·93 |
| ($B = -1220$) | 0·1855 | 1246·4 | 223·83 | 1·5218 | 10,156·8 | 221·73 |
| | 0·1880 | 1260·8 | 223·51 | 1·6365 | 10,880·1 | 220·82 |
| | 0·1924 | 1290·8 | 223·55 | 1·8395 | 12,241·7 | 220·93 |
| | 0·1949 | 1309·2 | 223·85 | | | |

$[R]_D = 11{\cdot}1$ cm.$^3$, our values for $A$ yield a mean $\mu$ of 3·90 D. Groves and Sugden[20] did not extrapolate their polarization measurements to $p = 0$, and since they worked in the pressure range from 6 to 10 cm. Hg, the $\mathscr{B}$ correction would add about 3 cm.$^3$ to their $\mathscr{A}$ at 80° and about 0·5 cm.$^3$ at 190°. These additions would lead to a small increase in $\mu$.

A graph of log $|\mathscr{B}|$ against $1/T$ is shown in Fig. 7, and the slope yields, through eqn. (7), $\Delta H_0 = -6{\cdot}8$ kcal. mole$^{-1}$, which is substantially larger than the value of $-3{\cdot}8$ kcal. mole$^{-1}$ at 100° obtained from a plot of log $(-B/T)$ against $1/T$. Fig. 8 shows how $-\Delta H_0$ decreases with rising temperature, which is to be expected for a loosely bound dimer, whereas eqn. (6) shows that $\langle\mu_{12}^2\rangle^{\frac{1}{2}}$ increases from 2·67 D at 80° to 4·62 D at 160°. The increasing polarity of the dimer offsets its decreasing stability as the temperature rises, producing an approximately linear graph in Fig. 7. These trends in $\Delta H_0$ and $\langle\mu_{12}^2\rangle^{\frac{1}{2}}$ are to be expected for a weakly bound dimer.

(c) *Arsenic Trifluoride.*—The molecular weight and saturated vapour pressure of arsenic trifluoride are sufficiently large to enable accurate measurements of $p$ and $V_m$ to be made. Thus $B$, as well as $_TP$, has been measured. The results are in Table 4 and Figs. 9 and 10.

TABLE 4.

Measurements on $AsF_3$.

| Temp. | $p$ (cm. Hg) | $10^5 V_m^{-1}$ (cm.$^{-3}$) | $10^6(\varepsilon-1)$ | $_TP$ (cm.$^3$ mole$^{-1}$) | $10^5 V_m^{-1}$ (cm.$^{-3}$) | $10^6(\varepsilon-1)$ | $_TP$ (cm.$^3$ mole$^{-1}$) |
|---|---|---|---|---|---|---|---|
| 80·61° | 9·557 | 0·4345 | 1657·5 | 127·08 | 1·0729 | 4116·3 | 127·71 |
| | 11·294 | 0·5137 | 1964·2 | 127·38 | 1·1844 | 4537·3 | 127·50 |
| | 11·514 | 0·5239 | 2001·1 | 127·24 | 1·4470 | 5529·2 | 127·14 |
| | 13·458 | 0·6130 | 2333·1 | 126·78 | 1·4529 | 5533·2 | 126·71 |
| | 14·164 | 0·6451 | 2461·9 | 127·11 | 1·7200 | 6575·4 | 127·15 |
| | | 0·5186 | 1980·4 | 127·20 | 2·2323 | 8530·6 | 127·02 |
| | | 0·6811 | 2602·1 | 127·24 | 2·5777 | 9847·0 | 126·92 |
| | | 0·7287 | 2775·7 | 126·86 | 3·1433 | 12,007·7 | 126·83 |
| | | 0·8837 | 3374·5 | 127·14 | 3·2363 | 12,393·0 | 127·12 |
| 159·88° | 11·112 | 0·4125 | 1317·0 | 106·37 | 0·7066 | 2257·6 | 106·42 |
| | 12·228 | 0·4521 | 1449·4 | 106·81 | 0·8806 | 2804·0 | 106·04 |
| | 12·673 | 0·4711 | 1502·4 | 106·25 | | | |
| | 14·354 | 0·5310 | 1702·2 | 106·80 | | | |

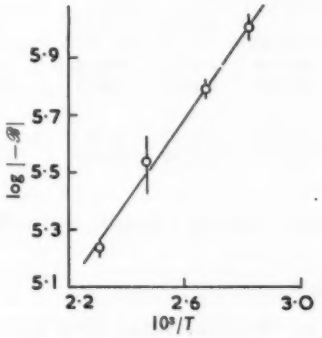



FIG. 7. The dependence of $\log|\mathscr{A}|$ on $1/T$ for $CH_3{\cdot}CN$.

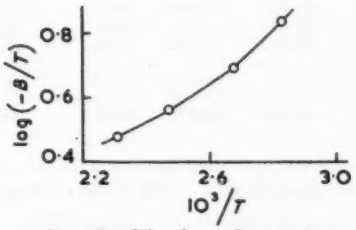



FIG. 8. The dependence of $\log(-B/T)$ on $1/T$ for $CH_3{\cdot}CN$.

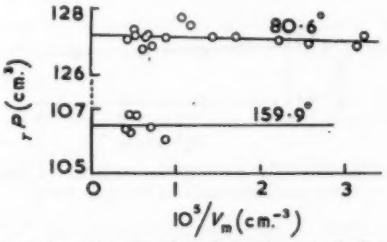



FIG. 9. The density dependence of the total polarization of $AsF_3$.

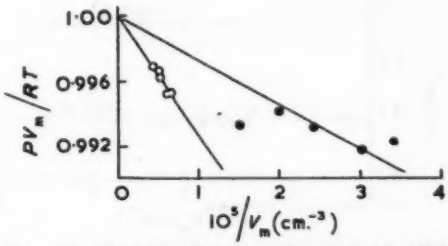



FIG. 10. The density dependence of $pV_m/RT$ for $AsF_3$ and $CHF_3$ at 80°.
● $CHF_3$ at 80·5°. ○ $AsF_3$ at 80·6°.

$T = 80{\cdot}61°$, $_TP = 127{\cdot}22 - 7900V_m^{-1}$, $\mathscr{A} = 127{\cdot}22 \pm 0{\cdot}10$ cm.$^3$ mole$^{-1}$, $\mathscr{B} = -7900 \pm 7000$ cm.$^6$ mole$^{-2}$, $B = -730 \pm 30$ cm.$^3$ mole$^{-1}$.

$T = 159{\cdot}88°$, $_TP = \mathscr{A} = 106{\cdot}45 \pm 0{\cdot}13$ cm.$^3$ mole$^{-1}$.

Hence $\alpha = 5{\cdot}45 \times 10^{-24}$ cm.$^3$, $\mu = 2{\cdot}57 \pm 0{\cdot}02$ D. This dipole moment is substantially less than the value $2{\cdot}815 \pm 0{\cdot}025$ D obtained [22] from the Stark effect on the microwave spectrum; the Stark energy was comparable with that of the nuclear quadrupoles, so the

[22] Shulman, Dailey, and Townes, *Phys. Rev.*, 1950, **78**, 145.

Stark splittings were not of the simple first-order type normally encountered in symmetric tops. However, we have verified the difficult quantum-mechanical analysis, so the disagreement is puzzling, and both the dielectric constant and the microwave experiments should now be repeated. If the disagreement turns out to be real, the two sets of data might be used jointly as evidence for the effect of an electric field on the electric field-gradient at the arsenic nucleus—this dependence is presumably a first-order one.

(d) *Fluoroform.*—Since fluoroform is a gas at room temperature and pressure, measurements of $p$, $V_m$, and $(\varepsilon - 1)$ were made (see Table 5), leading to $\mathscr{A}$, $\mathscr{B}$, and $B$. The precision of low-pressure readings enabled an accurate value of $\mathscr{A}$ to be found at 80·5° by means of eqn. (9), *viz.*, $\mathscr{A} = 55{\cdot}30 \pm 0{\cdot}03$ cm.$^3$ mole$^{-1}$, and this was then used with the polarizations in Table 5 to obtain $\mathscr{B}$. No attempt was made to evaluate $\mathscr{B}$ at 160·6°, the values of ${}_TP$ merely being averaged to give $\mathscr{A}$. The results are plotted in Figs. 10 and 11.

TABLE 5.

Measurements on $CHF_3$.

| Temp. | $p$ (cm. Hg) | $10^5 V_m^{-1}$ (cm.$^{-3}$) | $10^6(\varepsilon - 1)$ | ${}_TP$ (cm.$^3$ mole$^{-1}$) | $p$ (cm. Hg) | $10^5 V_m^{-1}$ (cm.$^{-3}$) | $10^6(\varepsilon - 1)$ | ${}_TP$ (cm.$^3$ mole$^{-1}$) |
|---|---|---|---|---|---|---|---|---|
| 80·49° | 32·300 | 1·5201 | 2513·1 | 55·06 | 66·094 | 3·0218 | 5001·3 | 55·08 |
| | 44·046 | 2·0090 | 3326·3 | 55·13 | 74·883 | 3·4217 | 5674·3 | 55·17 |
| | 53·412 | 2·4386 | 4039·9 | 55·15 | | | | |
| 160·57° | 34·971 | 1·2951 | 1821·4 | 46·85 | 60·944 | 2·2609 | 3158·3 | 46·52 |
| | 41·620 | 1·5458 | 2156·6 | 46·47 | 72·083 | 2·6739 | 3748·5 | 46·67 |
| | 49·219 | 1·8277 | 2556·3 | 46·58 | | | | |

$T = 80{\cdot}49°$, ${}_TP = 55{\cdot}30 - 6500 V_m^{-1}$, $\mathscr{A} = 55{\cdot}30 \pm 0{\cdot}03$ cm.$^3$ mole$^{-1}$, $\mathscr{B} = -6500 \pm 1400$ cm.$^6$ mole$^{-2}$, $B = -273 \pm 30$ cm.$^3$ mole$^{-1}$.

$T = 160{\cdot}57°$, ${}_TP = \mathscr{A} = 46{\cdot}62 \pm 0{\cdot}07$ cm.$^3$ mole$^{-1}$.

Hence $\alpha = 3{\cdot}28 \times 10^{-24}$ cm.$^3$, $\mu = 1{\cdot}65 \pm 0{\cdot}01$ D. Previous values of $\mu$ are $1{\cdot}64 \pm 0{\cdot}02$ D from microwave measurements [21] and 1·60 D from $\varepsilon$.[18]

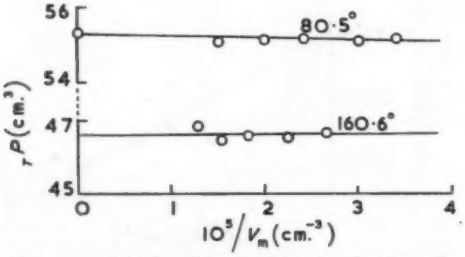



FIG. 11. The density dependence of the total polarization of $CHF_3$.

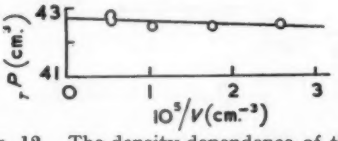



FIG. 12. The density dependence of the total polarization of $CHCl_3$ at 79·7°.

(e) *Chloroform.*—${}_TP$ was determined at 80°, by using direct pressure and density measurements at the three lowest densities (see Table 6). The results are plotted in Fig. 12.

TABLE 6.

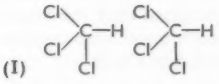
Measurements on $CHCl_3$.

| Temp. | $p$ (cm. Hg) | $10^5 V_m^{-1}$ (cm.$^{-3}$) | $10^6(\varepsilon - 1)$ | ${}_TP$ (cm.$^3$ mole$^{-1}$) | $10^5 V_m^{-1}$ (cm.$^{-3}$) | $10^6(\varepsilon - 1)$ | ${}_TP$ (cm.$^3$ mole$^{-1}$) |
|---|---|---|---|---|---|---|---|
| 79·70° | 11·494 | 0·5235 | 672·4 | 42·81 | 1·0386 | 1324·7 | 42·50 |
| | 11·892 | 0·5430 | 695·4 | 42·68 | 1·7638 | 2251·3 | 42·51 |
| | 12·210 | 0·5566 | 715·9 | 42·86 | 2·5808 | 3298·1 | 42·55 |

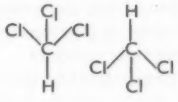
$_TP = 42{\cdot}76 - 10{,}800V_m^{-1}$, $\mathscr{A} = 42{\cdot}76 \pm 0{\cdot}08$ cm.$^3$ mole$^{-1}$, $\mathscr{B} = -11{,}000 \pm 6000$ cm.$^6$ mole$^{-2}$.

If $_DP = 25{\cdot}28$ cm.$^3$ mole$^{-1}$,[23] our $\mathscr{A}$ yields $\mu = 1{\cdot}00 \pm 0{\cdot}01$D, in agreement with the accepted value.[18]

The shapes of the arsenic trifluoride, fluoroform, and chloroform molecules are such that we had felt their $\mathscr{B}$s should have been positive, for we believed that arrangements of type (I) would be more stable than those of type (II); but the observed small negative $\mathscr{B}$s favour type (II). Measurements were also attempted on paraldehyde $(CH_3{\cdot}CHO)_3$,



(I)



(II)

because its shape and moment (1·44 D [24]) indicate [2] that it might have a substantial positive $\mathscr{B}$. However, decomposition into acetaldehyde occurred in our apparatus, even at temperatures as low as 79°, in spite of stringent precautions to remove acidic impurities; perhaps the tap greases, or the platinum of the gas cell, catalysed the depolymerization. Our dielectric-constant measurements provided a very sensitive method of detecting depolymerization, for three acetaldehyde molecules contribute much more than one of paraldehyde to $(\varepsilon-1)$. Decomposition at 79·1° and at 99·3° was slow enough for us to find evidence for a positive $\mathscr{B}$, and $\mathscr{A}$ values of 85 and 82 cm.$^3$ mole$^{-1}$, which are substantially larger than the previously determined values [24] of 80·8 and 78·8 cm.$^3$ mole$^{-1}$; however, decomposition seriously affected the accuracy of our measurements. Possibly 1,3,5-trioxan with its moment of 2 D, or $H_2O$ with its hydrogen bonds, has large positive $\mathscr{B}$s.

Our results have shown that highly polar vapours can show substantial deviations from the Clausius–Mossotti formula $_TP = \mathscr{A}$, even at pressures of a few cm. Hg. $\mathscr{B}/\mathscr{A}$ can be comparable to $B$, and sometimes, as in acetonitrile at low temperatures, can dominate the pressure dependence of $\frac{\varepsilon-1}{\varepsilon+2} \cdot \frac{RT}{p}$ [see eqn. (9)]. The simple polar molecules ($CH_3{\cdot}CN$, $AsF_3$, $CHF_3$, and $CHCl_3$) all apparently possess short-range intermolecular forces favouring antiparallel dipolar alignments as in (II); measurements of $\mathscr{B}$ at several temperatures provide a method of studying these forces, which are probably dependent upon the repulsions associated with molecular shape.

The authors are grateful to Dr. L. E. Sutton, F.R.S., for many very helpful discussions, and to the Rhodes Trustees for the award of a Scholarship (to R. E. R.)

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[*Received, May 24th,* 1961.]

[23] Maryott, Hobbs, and Gross, *J. Amer. Chem. Soc.*, 1941, **63**, 659.
[24] Le Fèvre, Mulley, and Smythe, *J.*, 1950, 290.

## 1081. *The Reactivity of Organophosphorus Compounds. Part VIII.*[1] *The Reactions of Chloramine-T with Triethyl Phosphorothiolate and Related Compounds.*

By J. I. G. Cadogan and H. N. Moulden.

Aqueous chloramine-T and triethyl phosphorothiolate give diethyl hydrogen phosphate, ethanesulphonic acid, *S*-ethyl-*S*-toluene-*p*-sulphonamido-*N*-toluene-*p*-sulphonylsulphidimine, and sulphuric acid in amounts varying according to the conditions. The mechanism of the reaction is discussed in the light of evidence collected from this reaction and those carried out with related thiolates and sulphidimines, and it is concluded that the sulphidimine is an intermediate product. Triethyl phosphorothionate and aqueous chloramine-T give triethyl phosphate, sulphur, and sulphuric acid.

Chloramine-T is known to react readily with organic sulphur compounds. Clarke, Kenyon, and Phillips [2] were the first to show that ethanethiol and aqueous chloramine-T gave *S*-ethyl-*S*-toluene-*p*-sulphonamido-*N*-toluene-*p*-sulphonylsulphidimine (II; R = Et). Alexander and McCombie [3] found that reaction with diethyl disulphide gave the same product. Bulmer and Mann [4] later showed that the thiol was oxidised by chloramine-T to the disulphide, which then reacted to give the sulphidimine. More recently Weibull [5] noted the formation of sulphidimines in the reactions between chloramine-B and *S*-esters of thioacetic, thiobenzoic, and thiosulphonic acid. The reactions between chloramine-T and phosphorothioates such as triethyl phosphoro-thiolate (I; R = Et) and -thionate [$(EtO)_3PS$] and related compounds are now described in this paper. The work was undertaken in the expectation that thiolates (I) would give the corresponding sulphidimines (II) which, as solids, would be acceptable derivatives of the type required for another investigation.

It has now been shown that fission of the phosphorus–sulphur bond occurs when triethyl phosphorothiolate (I; R = Et) reacts with aqueous chloramine-T. The *S*-ethyl group appears as ethanesulphonic acid and *S*-ethyl-*S*-toluene-*p*-sulphonamido-*N*-toluene-*p*-sulphonylsulphidimine (II; R = Et). Inorganic sulphate, toluene-*p*-sulphonamide, and diethyl hydrogen phosphate are also produced in the reaction, which is heterogeneous when carried out in water. The addition of ethanol as a homogenising agent affects the relative proportions, but not the nature, of the products formed; the proportions also vary with the temperature and the relative proportions of the reactants, as shown in the Table. In unbuffered solution there is an induction period followed by rapid reaction during which the pH drops from 8, that of aqueous chloramine-T, to 2.

The reaction with *S*-benzyl diethyl phosphorothiolate (I; R = $Ph{\cdot}CH_2$), carried out in boiling aqueous ethanol, gives benzyl alcohol and sulphate (81%), but no sulphidimine.

$(EtO)_2PO{\cdot}SR$ (I) $\quad p\text{-}C_6H_4Me{\cdot}SO_2{\cdot}N{:}SR{\cdot}NH{\cdot}SO_2{\cdot}C_6H_4Me\text{-}p$ (II) $\quad (EtO)_2PO{\cdot}NH{\cdot}SO_2{\cdot}C_6H_4Me\text{-}p$ (III)

In the reaction with phosphorothiolates it was considered possible that the sulphidimine was formed by chlorination of the ester followed by reaction of the products of chlorination with chloramine-T. Sulphenyl trichlorides and sulphenyl chlorides [6] are considered to be intermediates in the chlorination of phosphorothiolates. Neither the reaction between ethanesulphenyl trichloride and chloramine-T, nor that with toluene-*p*-sulphonamide, gave the sulphidimine. The sulphidimine (II; R = Et) was isolated, however, with ethanesulphonic acid, after reaction of ethanesulphenyl chloride and chloramine-T in

[1] Part VII, Cadogan and Moulden, *J.*, 1961, 3080.
[2] Clarke, Kenyon, and Phillips, *J.*, 1930, 1225.
[3] Alexander and McCombie, *J.*, 1932, 2087.
[4] Bulmer and Mann, *J.*, 1945, 666.
[5] Weibull, *Arkiv Kemi*, 1951, **3**, 171.
[6] Stirling, *J.*, 1957, 3597.

Reactions of chloramine-T with thiolates and sulphidimines.[a]

| Compound (P) | $(EtO)_2PO\cdot SEt$ | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Molar ratio, | | | | | | | | | $X$[i] | $Y$ | |
| CT/P | 1 | 2 | 2 | 2 | 2[b] | 4 | 4[c] | 4[d] | 4·2 | 2[g] | 2 | $Z$ 2 |
| Temp. | 20 | 20 | 20 | 80 | 20 | 20 | 80 | 20 | 80 | 100 | 80 | 100 |
| Time (hr.) | 48 | 48 | 48 | 0·25 | 18 | 24 | 0·25 | 0·5 | 0·5 | 28 | 0·25 | 0·25 |
| EtOH (v/v) | 0 | 0 | 30 | 30 | 30 | 0 | 30 | 0 | 20 | 0 | 20 | 0 |
| $Ar\cdot SO_2\cdot NH_2$[e] | 0·78 | 0·74 | 0·49 | 0·86 | 0·96 | 0·74 | 0·90 | 0·91 | 0·99 | 3·4[f] | 3·0[f] | 3·37 |
| Sulphidimine | 0·22 | 0·20 | 0·53 | 0·09 | 0 | 0·20 | 0·02 | 0·02 | 0 | 0 | 0·09 | 0 |
| $SO_4$ | 0·02 | 0·03 | 0·03 | 0·05 | 0·01 | — | 0·44 | — | 0·81 | 0·60 | 0·45 | 0·98 |
| $Et\cdot SO_3H$ | 0·32 | 0·30 | — | — | — | — | — | — | — | — | 0·14 | — |
| $(EtO)_2PO_2H$ | 0·79 | 0·77 | — | — | — | — | — | — | 0·99[h] | — | — | — |
| Thiolate recovered (%) | 56 | 25 | 17 | 29 | 12 | 0 | 0 | 0 | 0 | — | — | — |

*X*, $(EtO)_2P(O)\cdot S\cdot CN_2Ph$. *Y*, $ArSO_2\cdot NH\cdot SEt{:}N\cdot SO_2Ar$. *Z*, $ArSO_2\cdot NH\cdot S(CH_2Ph){:}N\cdot SO_2Ar$.
[a] Products given in moles per mole of sulphur compound reacted. [b] In the presence of HCl; $Et\cdot SO_2H$ was also formed. [c] $(EtO)_2PO$ (0·07 mole/mole) was also formed. [d] In the presence of HCl; $Et\cdot SO_2Cl$ (55%) was also formed. [e] Moles/mole of chloramine-T. [f] Moles/mole of sulphidimine. [g] In the presence of HCl. [h] Impure. [i] $Ph\cdot CH_2\cdot OH$ (0·44 mole/mole) was also isolated. [j] $Ph\cdot CH_2\cdot OH$ (0·26 mole/mole) was also isolated.

aqueous ethanol, a small quantity of impure diethyl disulphide being also obtained. Disulphides [7] and thiolsulphonates [8] have been isolated after reaction of sulphenyl halides and alcohols, so the formation of the sulphidimine in the reaction of sulphenyl chloride with chloramine-T can be rationalised. It is particularly significant in this connection that the yield of sulphidimine from triethyl phosphorothiolate was greatest when the reaction was carried out in aqueous ethanol. Further, a small quantity of diethyl disulphide was detected in the products of the reaction of two mol. of triethyl phosphorothiolate with one of chloramine-T; the sulphidimine (II; R = Et) and unchanged phosphorothiolate were also isolated. It is possible therefore that some, at least, of the sulphidimine is formed by way of the disulphide.

Weibull [5] isolated *N*-benzoylbenzenesulphonamide from the reaction products of *S*-cyclohexyl thiobenzoate and chloramine-B. A re-investigation, with chloramine-T and *S*-ethyl thiobenzoate, has confirmed this and, in addition, toluene-*p*-sulphonamide, the sulphidimine (II; R = Et), benzoic acid, and inorganic sulphate were isolated, and the odour of benzoyl chloride was apparent after the reactants had been mixed.

In contrast, the analogous diethyl *N*-*p*-toluenesulphonylphosphoramidate (III) was not isolated from or detected in reactions with triethyl phosphorothiolate, although a careful search was made. The amidate (III) was shown to be unaffected by boiling aqueous-ethanolic chloramine-T, and was recovered from a reaction mixture of triethyl phosphorothiolate and chloramine-T to which it had been added. It thus appears that attack on the phosphorus atom by the *N*-chlorotoluene-*p*-sulphonamide anion occurs only to a very small extent, if at all, providing a further example of the reduced electrophilicity of phosphoryl phosphorus compared with carbonyl carbon.

As a result of the pH change during the reaction of aqueous chloramine-T with thiolates, it is necessary to examine the consequence of such a change on chloramine-T.

Chloramine-T, in aqueous solution, is partly converted into toluene-*p*-sulphonamide and dichloramine-T by the addition of acid. This has been demonstrated for chloramine-B by Zil'berg.[9] Morris, Salazar, and Wineman [10] have assumed that the following equibria exist in slightly acid solutions and have calculated equilibrium constants:

$$H_2O + p\text{-}C_6H_4Me\cdot SO_2\cdot NCl_2 \rightleftharpoons p\text{-}C_6H_4Me\cdot SO_2\cdot NHCl + HOCl$$

$$2p\text{-}C_6H_4Me\cdot SO_2\cdot NHCl \rightleftharpoons p\text{-}C_6H_4Me\cdot SO_2\cdot NCl_2 + p\text{-}C_6H_4Me\cdot SO_2\cdot NH_2$$

[7] Zinke and Farr, *Annalen*, 1912, **391**, 57.
[8] Zinke and Esmayer, *Ber.*, 1918, **51**, 751.
[9] Zil'berg, *J. Gen. Chem. U.S.S.R.*, 1946, **16**, 2145.
[10] Morris, Salazar, and Wineman, *J. Amer. Chem. Soc.*, 1948, **70**, 2036.

Also, chloramine-T in the presence of hydrochloric acid has been used to chlorinate acetanilide, and Orton and Bradfield [11] considered the chlorinating agent to be molecular chlorine. Thus, in the reaction with phosphorothiolates, when the reaction mixture becomes acidic several reactive species are almost certainly involved and may include chlorine, *N*-chlorotoluene-*p*-sulphonamide, and the $H_2OCl^+$ ion produced from hypochlorous acid or by hydrolysis of *N*-chlorotoluene-*p*-sulphonamide.

Stirling [6] found that aqueous chlorination of triethyl phosphorothiolate produced ethanesulphonyl chloride and diethyl hydrogen phosphate, and suggested the following mechanism:

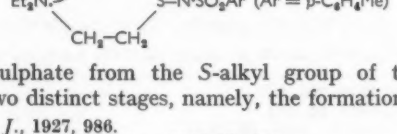
$$(EtO)_2PO{\cdot}SEt \xrightarrow{Cl_2} \begin{cases} (EtO)_2PO{\cdot}Cl \longrightarrow (EtO)_2PO_2H \\ + \\ EtSCl \xrightarrow{Cl_2} Et{\cdot}SCl_3 \xrightarrow{H_2O} Et{\cdot}SO_2H \xrightarrow{Cl_2} Et{\cdot}SO_2Cl \end{cases}$$

Since molecular chlorine is almost certainly present when the reaction mixture is acidic, it is possible that the formation of ethanesulphonic acid in reactions with chloramine-T proceeds by a similar mechanism. This is supported by the isolation of ethanesulphonyl chloride from a reaction in acid solution between chloramine-T and triethyl phosphorothiolate, and the isolation of triethyl phosphate from a reaction carried out in aqueous ethanol is considered to be evidence for the formation of diethyl phosphorochloridate at one stage of the reaction. Ethanesulphinic acid, isolated as benzyl ethyl sulphone, was also a product of the reaction of chloramine-T and triethyl phosphorothiolate in the presence of hydrochloric acid, and, in fact, Stirling [6] found that sulphinic acids were products of partial aqueous chlorination of phosphorothiolates. It is probable therefore that that part of the reaction between chloramine-T and triethyl phosphorothiolate which occurs at low pH is initially a chlorination, although participation of other species mentioned above cannot be excluded.

Epstein and Lordi [12] have shown that alkaline hydrolysis of triethyl phosphorothiolate to ethanethiol and diethyl hydrogen phosphate is catalysed by hypochlorite ion. It was therefore possible that the reaction between chloramine-T and phosphorothiolate also involves catalysis [equation (1)] by the $Ar{\cdot}SO_2{\cdot}NCl^-$ ion or a similar species. Ethanethiol, which would be produced by such a reaction, is known to react with chloramine-T to give the sulphidimine (II; R = Et). Such catalysis was, however, shown not to occur.

$$(EtO)_2PO{\cdot}SR \xrightarrow{Ar{\cdot}SO_2{\cdot}NCl^-} RS^- + (EtO)_2PO{\cdot}NCl{\cdot}SO_2Ar \xrightarrow{HO^-} (EtO)_2PO_2H + Ar{\cdot}SO_2{\cdot}NCl^- \quad . \quad (1)$$

Reaction between triethyl phosphorothiolate and chloramine-T in aqueous sodium hydrogen carbonate was very slow and no sulphidimine was formed. Similarly, *S*-2-diethylaminoethyl thiobenzoate, which acts as its own buffer, did not react in 20 hr., whereas the hydrochloride of this base reacted very rapidly with aqueous chloramine-T to give *S*-2-diethylaminoethyl-*S*-toluene-*p*-sulphonamido-*N*-toluene-*p*-sulphonylsulphidimine (II; $R = Et_2N{\cdot}CH_2{\cdot}CH_2$). It can be concluded, therefore, that sulphidimine formation occurs in acid solution, *i.e.*, under conditions where products derived by chlorination of the ester have been shown to be formed. It is noteworthy that the sulphidimine (II; $R = Et_2N{\cdot}CH_2{\cdot}CH_2$) crystallised directly from hydrochloric acid solution and not as the hydrochloride, showing that zwitterion formation had occurred.




The formation of sulphate from the *S*-alkyl group of the phosphorothiolates is considered to involve two distinct stages, namely, the formation of the sulphidimine (II)

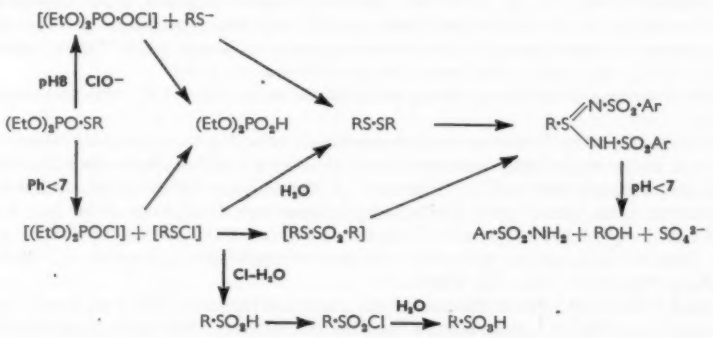
[11] Orton and Bradfield, *J.*, 1927, 986.
[12] Epstein and Lordi, *J. Amer. Chem. Soc.*, 1958, **80**, 509.

and its subsequent reaction with chloramine-T (or its transformation products) in acid solution. This follows from the observations that both *S*-benzyl- (II; R = Ph·$CH_2$) and *S*-ethyl-*S*-toluene-*p*-sulphonamido-*N*-toluene-*p*-sulphonylsulphidimine (II; R = Et) reacted readily with chloramine-T in unbuffered and in acid solution, but not in alkaline solution, to give sulphate. Thus during the reaction of phosphorothiolates with chloramine-T, when the reaction medium becomes acidic, the reactions of the remaining chloramine-T (or its equivalent in acid solution) with phosphorothiolate and sulphidimine are in competition. The variations in yields of products with changes in conditions are explicable on this basis.

No identifiable intermediate products of the reaction of chloramine-T and the sulphidimine (II; R = Et) could be isolated, but a hygroscopic mixture was obtained which gave more sulphate on treatment with chloramine-T. We have no evidence that the initial stages of the decomposition of the sulphidimine (II; R = Et) involve fission of sulphur–nitrogen bonds, since ethanesulphinic acid, ethanesulphonic acid, and ethanesulphonyl chloride, possible intermediates in such a reaction, give only traces of sulphate under these conditions.

Weibull [5] noted the formation of sulphate in reactions of chloramine-B with dicyclohexyl disulphide and with *S*-cyclohexyl thioacetate and thiobenzoate but proposed a mechanism for its formation which neglected the reaction between sulphidimine and chloramine-T.

Our suggestions concerning the reaction between phosphorothiolates and chloramine-T can be summarised as annexed, where hypothetical intermediates are indicated in square brackets.




Spontaneous hydrolysis of chloramine-T to give hypochlorous acid is first invoked, followed by hypochlorite-ion catalysis of the hydrolysis at pH 8 of the ester to give thiol anion and diethyl hydrogen phosphate.[12] This hydrolysis is relatively slow at pH 8 but is replaced as the main mode of decomposition as soon as the medium becomes acid. At this point the many possible reactions referred to above can become operative, including aqueous chlorination leading to the formation of disulphide, thiosulphonate, and sulphenyl chloride, all of which react with chloramine-T to give the sulphidimine. The possibility that the sulphidimine can be formed by way of *N*-ethanesulphenyltoluene-*p*-sulphonamide exists but has not been confirmed by isolation of this substance as an intermediate product in any of our experiments.

Triethyl phosphorothionate, $(EtO)_3PS$, with chloramine-T gives triethyl phosphate, sulphur, inorganic sulphate, and toluene-*p*-sulphonamide. When the proportion of chloramine-T to ester and the temperature are both increased, a greater yield of sulphate is obtained; chloramine-T and sulphur in boiling water give good yields of sulphate, and it is probably this reaction which accounts for the increased yield of sulphate.

## Experimental

Extracts were dried over magnesium sulphate. The light petroleum used had b. p. 40—60°. A Perkin-Elmer " Fraktometer " model 116, fitted with a high-sensitivity dual thermal conductivity detector, was used. The response was tested by analysis of mixtures of known composition and found to be satisfactory. The column packings were " A," di-n-decyl phthalate on Celite, and " C " Silicone oil D.C. 200 on Celite.

*Preparation of Compounds.*—Triethyl phosphorothiolate, b. p. 95°/12 mm., $n_D^{25}$ 1·4553 (lit.,[6] b. p. 79°/1·3 mm., $n_D^{25}$ 1·4570), was prepared from sodium *OO*-diethyl phosphorothiolate and ethyl bromide. Triethyl phosphorothionate, b. p. 121—124°/60 mm., $n_D^{25}$ 1·4464 (lit.,[13] b. p. 95°/12 mm., $n_D^{20}$ 1·4480 [14]), was obtained after addition of sulphur to triethyl phosphite at room temperature. *S*-Benzyl diethyl phosphorothiolate, b. p. 130°/0·2 mm., $n_D^{25}$ 1·5234 (lit.,[6] b. p. 130°/0·2 mm., $n_D^{25}$ 1·5229), was prepared from benzyl chloride and sodium *OO*-diethyl phosphorothioate in ethanol. *S*-Ethyl thiobenzoate was prepared by boiling thiobenzoic acid (50 g.), sodium ethoxide solution (sodium, 8·33 g.; ethanol, 250 ml.) and ethyl iodide (64 g.) for 90 min.; removal of the low-boiling components followed by treatment with water gave the ester (15·5 g.), b. p. 128—130°/12 mm., $n_D^{25}$ 1·5703 (Wolfrom and Karabinos [15] report $n_D^{20}$ 1·5721).

*Ethanesulphenyl Chloride.*[16]—Diethyl disulphide [17] (5·0 g.) was stirred in methylene chloride (20 ml.) at −20° while a solution of chlorine (3·0 g.) in methylene chloride (50 ml.) was added. Distillation gave ethanesulphenyl chloride, b. p. 20—30°/14 mm. (2·44 g.). Ethanesulphenyl trichloride was prepared by chlorination of ethanesulphenyl chloride in carbon tetrachloride at −20° as described by Douglass and Poole.[18] *S*-Ethyl-*S*-toluene-*p*-sulphonamido-*N*-toluene-*p*-sulphonylsulphidimine, m. p. 189° (decomp.), was prepared by Clarke, Kenyon, and Phillips's method; [2] they reported m. p. 189°. *S*-Benzyl-*S*-toluene-*p*-sulphonamido-*N*-toluene-*p*-sulphonylsulphidimine, m. p. 177—178° (decomp.), was prepared from chloramine-T and dibenzyl disulphide by the method of Bulmer and Mann,[4] who reported m. p. 171—171·5°.

Reduction of ethanesulphonyl chloride with aqueous sodium sulphite [19] gave sodium ethanesulphinate (20%), characterised as benzyl ethyl sulphone, m. p. 84°.

Diethyl *N*-toluene-*p*-sulphonyl phosphoramidate, m. p. 106—107°, was prepared by Ratz's method.[20]

S-2-*Diethylaminoethyl*-S-*toluene*-p-*sulphonamido*-N-*toluene*-p-*sulphonylsulphidimine*.—Iodine (10·3 g.) was added to 2-diethylaminoethanethiol (10·8 g.) and sodium ethoxide [from sodium (1·87 g.) and ethanol (100 ml.)]. Removal of the solvent followed by addition of water and extraction with ether gave bis-2-diethylaminoethyl disulphide (8·16 g.), b. p. 106—114°/0·05 mm., $n_D^{25}$ 1·5026 (Found: C, 54·6; H, 10·5. Calc. for $C_{12}H_{28}N_2S_2$: C, 54·5; H, 10·7%); [*dimethiodide*, m. p. 213—214° (from methanol–ether) (Found: C, 30·7; H, 6·1. $C_{14}H_{34}I_2N_2S_2$ requires C, 30·7; H, 6·25%)].

The disulphide (1·32 g.) in methanol (10 ml.), and chloramine-T (5·821 g., 4 mol.) in methanol (20 ml.) and water (50 ml.), were stirred together for 30 min. S-2-*Diethylaminoethyl*-S-*toluene*-p-*sulphonamido*-N-*toluene*-p-*sulphonylsulphidimine* (2·50 g.), which separated from acid solution, crystallised from ethanol and then had m. p. 189—190° (decomp.) (Found: C, 51·4; H, 6·4; S, 19·9. $C_{29}H_{39}N_3O_4S_3$ requires C, 50·95; H, 6·2; S, 20·4%).

*S*-2-Diethylaminoethyl thiobenzoate, b. p. 110°/0·1 mm., $n_D^{25}$ 1·5460, was prepared as described by Stirling [21] who reported $n_D^{25}$ 1·5465.

*Reactions with Chloramine-T.*—Some of the reactions carried out are described in detail below. Where reaction conditions or methods of isolation of products are only slightly different, details have not been given. The reaction conditions and results of these experiments are given in the Table. In these cases the identities of the products were confirmed by mixed m. p. determinations and/or comparison of infrared spectra.

[13] Strecker and Spitaler, *Ber.*, 1926, 1772.
[14] Arbuzov and Vinogradova, *Izvest. Akad. Nauk S.S.S.R.*, 1947, 459.
[15] Wolfrom and Karabinos, *J. Amer. Chem. Soc.*, 1946, **68**, 1455.
[16] Cf. Britzinger and Langheck, *Chem. Ber.*, 1953, **86**, 557.
[17] Vogel and Cowan, *J.*, 1943, 16.
[18] Douglass and Poole, *J. Org. Chem.*, 1957, **22**, 536.
[19] Cf. Smiles and Berl, *Org. Synth.*, Coll. Vol. I, p. 7.
[20] Ratz, *J. Org. Chem.*, 1957, **22**, 372.
[21] Stirling, *J.*, 1958, 4524.

*Reaction of Triethyl Phosphorothiolate with Aqueous Chloramine-T.*—(a) 1 : 1 *Mole.* Chloramine-T (28·2 g.), in water (250 ml.) at 5°, was added during ½ hr. to a stirred suspension of triethyl phosphorothiolate (20 g.) in water (20 ml.). The mixture was stirred for a further 10 min., during which the pH of the mixture changed from 8 to 2 and a white solid separated. The white solid liberated iodine from potassium iodide but the supernatant liquid gave no reaction. The mixture was set aside for 48 hr. at room temperature and then boiled under reflux for 10 min. The white crystals which separated on cooling gave no reaction with potassium iodide and were filtered off and washed with light petroleum (4 × 60 ml.). Recrystallisation from dilute sodium carbonate solution gave toluene-*p*-sulphonamide (10·12 g.), m. p. and mixed m. p. 139—140°. Extraction of the mother liquors with ether gave more sulphonamide (1·41 g.), m. p. and mixed m. p. 138—139°. The mother liquors were acidified with hydrochloric acid; the white precipitate was fractionally crystallised from ethanol, to give *S*-ethyl-*S*-toluene-*p*-sulphonamido-*N*-toluene-*p*-sulphonylsulphidimine (3·90 g.), m. p. and mixed m. p. 186—187° (decomp.), and a white solid (0·24 g.), m. p. 126—140° (decomp.), shown by its infrared spectrum to be impure sulphidimine. Extraction of the acid mother liquors with ether gave toluene-*p*-sulphonamide (0·69 g.), m. p. 130—132°. The filtered reaction mixture was made alkaline ($Na_2CO_3$) and extracted continuously with ether. The ether extracts, combined with the light petroleum washings of the sulphonamide fraction, were distilled, giving a colourless liquid (11·49 g.), b. p. 30—50°/0·1 mm., $n_D^{25}$ 1·4584, and left a black residue (1·39 g.), b. p. >120°/0·1 mm., which on crystallisation from aqueous ethanol yielded toluene-*p*-sulphonamide (1·07 g.), m. p. 129—137°, whose identity was confirmed by its infrared spectrum. The distillate was shown to contain 97 ± 1% of triethyl phosphorothiolate, by comparison of its infrared spectrum with that of authentic material (method of Augood, Hey, and Williams [22]) in chloroform with optical density measured at 1161, 1391, and 1441 cm.$^{-1}$. However, the material absorbed strongly at 1129 and 1323 cm.$^{-1}$. Triethyl phosphorothiolate has no absorption bands at these frequencies. Gas–liquid chromatography of this fraction (2 m. column, packing "C," at 190°) confirmed that it contained 97% of triethyl phosphorothiolate and revealed the presence of four other components having slightly lower b. p.

The reaction mixture, which had been extracted with ether, was made just acid with hydrochloric acid and extracted with ether (5 × 50 ml.). The material in the extracts, on crystallisation from benzene–light petroleum, gave toluene-*p*-sulphonamide (0·08 g.), m. p. 130—133°, and an oil (0·19 g.) whose infrared spectrum was consistent with that of a mixture of toluene-*p*-sulphonamide and diethyl hydrogen phosphate. No diethyl *N*-toluene-*p*-sulphonylphosphoramidate was isolated, and its presence could not be detected by examination of the infrared spectrum of the oil. After addition of sodium chloride and an excess of hydrochloric acid, the aqueous reaction mixture was continuously extracted with ether (24 hr.). The ether extracts gave diethyl hydrogen phosphate (5·46 g.) b. p. 120—140°/0·01 mm., $n_D^{25}$ 1·4122, which was identified by comparison of its infrared spectrum with that of authentic material. The aqueous layer was then neutralised with sodium carbonate and evaporated to dryness. Ethanol extracts of the residue gave sodium ethanesulphonate (2·15 g.) (Found: S, 21·9. Calc. for $C_2H_5NaO_3S,H_2O$: S, 21·3%). Its identity was confirmed by comparison of its infrared spectrum with that of authentic material. The residue from the ethanol extraction was dissolved in dilute hydrochloric acid and treated with aqueous barium chloride, to give barium sulphate (0·223 g.).

Other experiments were carried out with the following molar ratios of thiolate to chloramine-T: 1 : 2; 1 : 2 in aqueous ethanol at 20° and 80°; 1 : 4 in aqueous ethanol at 80°. The products were isolated in the usual way and the results are summarised in the Table given above.

(b) 1 : 2 *Moles, with added diethyl N-toluene-*p*-sulphonylphosphoramidate.* Triethyl phosphorothiolate (10·0 g.) and chloramine-T (28·2 g.), in water (250 ml.), were allowed to react as described above, in the presence of an aqueous solution of the amidate (2·0 g.) which had been neutralised with sodium carbonate (0·35 g.). The aqueous sodium carbonate extracts of the sulphonamide–sulphidimine fraction, filtered off from the reaction mixture, were shown to be free from amidate by fractional crystallisation from ethanol and by spectroscopic examination of each fraction. After unchanged triethyl phosphorothiolate had been extracted the basified

[22] Augood, Hey, and Williams, *J.*, 1953, 44.

reaction mixture was then strongly acidified with hydrochloric acid and extracted continuously with ether (24 hr.). The ether extracts was evaporated and the residue dissolved in saturated aqueous sodium hydrogen carbonate and continuously extracted with ether (24 hr.). The aqueous layer was acidified with hydrochloric acid and extracted with ether (4 × 50 ml.), giving a colourless oil (1·89 g.) whose infrared spectrum was identical with that of the amidate. The oil crystallised from dilute hydrochloric acid, containing sodium chloride, and gave the amidate, m. p. and mixed m. p. 102—104°.

(c) 2 : 1 *Moles.* The ester (10·0 g.) and chloramine-T (7·05 g.) were allowed to react in water (100 ml.) for 10 min. at room temperature. The mixture was extracted with light petroleum (4 × 50 ml.). Distillation of the water-washed extracts gave a fraction (4·58 g.), b. p. 100—125°/15 mm., $n_D^{25}$ 1·4545, which contained triethyl phosphorothiolate (90%), diethyl disulphide (3%), and traces of light petroleum, as shown by gas–liquid chromatography as described above. *S*-Ethyl-*S*-toluene-*p*-sulphonamido-*N*-toluene-*p*-sulphonylsulphidimine (1·02 g.), m. p. and mixed m. p. 185° (decomp.), was isolated from a similar experiment carried out with the ester (5·0 g.) in 10% aqueous ethanol (30 ml.).

(d) 1 : 2 *Moles, at* 20°, *with added hydrochloric acid.* The reaction was carried out with the ester (5 g.) and hydrochloric acid (1·4 g.) in aqueous ethanol, working up being in the usual way. The results are summarised in the Table. The fraction (4·54 g.) containing sodium diethyl phosphate, on treatment with benzyl bromide in aqueous ethanol at 90°, gave benzyl ethyl sulphone, m. p. and mixed m. p. 81—82°. After a reaction with 4 equiv. of chloramine-T (see Table) the precipitate of sulphonamide and sulphidimine was washed with light petroleum. Distillation of the dried washings gave ethanesulphonyl chloride (55%), b. p. 72—75°/20 mm., $n_D^{25}$ 1·4470 (anilide, m. p. and mixed m. p. 56°).

*Reaction of* S-*Benzyl Diethyl Phosphorothiolate with Aqueous Chloramine*-T.—The ester (5 g.) was used in 20% aqueous ethanol (300 ml.); details of products and conditions are given in the Table. Extraction of the basified reaction mixture with chloroform (8 × 100 ml.) gave benzyl alcohol (0·90 g.), b. p. 90—100°/20 mm. (3,5-dinitrobenzoate, m. p. and mixed m. p. 113°). No sulphidimine was detected. Benzyl alcohol was also isolated from a complementary experiment (see Table for details) with the sulphidimine (10·0 g.) in water (250 ml.).

*Reaction of* S-*Ethyl Thiobenzoate with Chloramine*-T.—Chloramine-T (21·2 g.) in water (270 ml.) was added slowly to a stirred suspension of *S*-ethyl thiobenzoate (5·0 g.) in water (10 ml.) at room temperature. White crystals appeared after 5 min. and there was an odour of benzoyl chloride. The mixture was left for 48 hr. at room temperature and then boiled under reflux, for 10 min. The solid which separated on cooling was collected, washed with light petroleum, and extracted with saturated aqueous sodium hydrogen carbonate. This left toluene-*p*-sulphonamide (3·31 g.), m. p. and mixed m. p. 136—137°. The petroleum washings gave benzoic acid (0·85 g.), m. p. and mixed m. p. 122—122·5°. The sodium hydrogen carbonate extracts were washed with chloroform, and the washings gave toluene-*p*-sulphonamide (2·73 g.), m. p. 136—138° (from aqueous ethanol). The alkaline solution was acidified with hydrochloric acid and the white precipitate was collected. The filtrate, on extraction with methylene dichloride, gave benzoic acid (1·0 g.), m. p. and mixed m. p. 120—121° (from water). The white precipitate crystallised from ethanol, giving *S*-ethyl-*S*-toluene-*p*-sulphonamido-*N*-toluene-*p*-sulphonylsulphidimine (2·67 g.), m. p. and mixed m. p. 185—186° (decomp.). The mother liquors were evaporated to dryness and the residue extracted with boiling water, leaving *N*-benzoyltoluene-*p*-sulphonamide (1·05 g.), m. p. and mixed m. p. 146—147° (from aqueous ethanol). The aqueous extract was fractionally crystallised from aqueous ethanol, giving more *N*-benzoyltoluene-*p*-sulphonamide (0·05 g.), m. p. and mixed m. p. 145—146°, and benzoic acid (0·33 g.), m. p. 110° undepressed on admixture with authentic material. The filtered reaction mixture was neutralised with sodium hydrogen carbonate and extracted with ether, to give toluene-*p*-sulphonamide (0·75 g.), m. p. 138—140° (from aqueous ethanol). The aqueous layer was evaporated under reduced pressure and the residue extracted with ethanol (2 × 50 ml.). The remaining solid was dissolved in dilute hydrochloric acid and treated with barium chloride, to give barium sulphate (0·296 g.). The ethanol extracts were reduced in volume to about 10 ml. and treated with ether, giving an unidentified white precipitate (1·05 g.) which recrystallised from ethanol–ether (Found: C, 26·4; H, 3·2; S, 16·35; Na, 19·0%).

*Reaction of Ethanesulphenyl Chloride with Aqueous Chloramine*-T.—Chloramine-T (8·89 g.) in 30% aqueous ethanol (90 ml.) was added to ethanesulphenyl chloride (3·05 g.). The orange colour of the sulphenyl chloride rapidly disappeared and heat was evolved. The mixture was

left for 5 days at room temperature and a white precipitate was collected. This crystallised from dilute aqueous sodium carbonate, giving toluene-*p*-sulphonamide (3·74 g.), m. p. and mixed m. p. 138°, and the mother liquor, on acidification with hydrochloric acid, yielded *S*-ethyl-*S*-toluene-*p*-sulphonamido-*N*-toluene-*p*-sulphonylsulphidimine (0·20 g.), m. p. and mixed m. p. 185—186° (decomp.). Chloroform extracts of the filtrate were digested with light petroleum and gave a fraction (0·2 g.), b. p. 80—140°/760 mm., whose infrared spectrum showed the presence of diethyl disulphide. Toluene-*p*-sulphonamide (0·50 g.), m. p. 137—138°, was extracted from the residue from the light petroleum extracts with aqueous ethanol. The extracted reaction mixture was neutralised with sodium carbonate and evaporated to dryness. Ethanol extracts gave sodium ethanesulphonate (1·77 g.); the residue, on treatment with barium chloride, gave barium sulphate (0·054 g.).

Reaction of freshly prepared ethanesulphenyl trichloride with aqueous-ethanolic toluene-*p*-sulphonamide or aqueous-ethanolic chloramine-T gave no sulphidimine.

*Reactions of* S-*Ethyl*-S-*toluene*-p-*sulphonamido*-N-*Toluene*-p-*sulphonylsulphidimine*.—(a) *With chloramine*-T. The details of the reaction carried out with the sulphidimine (10·0 g.) are given in the Table. The working up was standard. Evaporation of the ethanol extracts of the residue gave a hygroscopic solid mixture (3·0 g.). A portion (1·0 g.) gave sodium ethanesulphonate (0·13 g.). Another portion (1·28 g.) was extracted with acetone, and a solid was precipitated from the extracts on the addition of ether; recrystallisation from acetone–ether gave a very hygroscopic, unidentified substance (0·28 g.) (Found: C, 36·9; H, 4·6; N, 4·5; S, 22·3; Na, 8·3%). A third portion (1·0 g.) of the hygroscopic mixture (which contained no sulphate) was boiled with chloramine-T (7·05 g.) in water (100 ml.) for 16 hr.: barium sulphate (0·42 g.) and toluene-*p*-sulphonamide (3·48 g.) were isolated.

(b) *With chloramine*-T *and hydrochloric acid*. Hydrochloric acid (2·0 g.; *d* 1·18) was added to a solution of the sulphidimine (5·0 g.) and chloramine-T (7·05 g.) in water (150 ml.) (pH 2), and the mixture was boiled under reflux for 28 hr. Toluene-*p*-sulphonamide (7·21 g.) and barium sulphate (1·679 g.) were isolated as described above.

The sulphidimine was partially hydrolysed to toluene-*p*-sulphonamide and ethanesulphonic acid after treatment with hydrochloric acid alone under these conditions, but no sulphate was formed. The sulphidimine was recovered quantitatively after only 15 min. under the same conditions, and after being boiled (19 hr.) with aqueous chloramine-T (2 mol.) in the presence of sodium carbonate.

*Reaction of Chloramine*-T *with* S-2-*Diethylaminoethyl Thiobenzoate Hydrochloride*.—*S*-2-Diethylaminoethyl thiobenzoate (1 mol.) was dissolved in an excess of dilute hydrochloric acid, and aqueous chloramine-T (2 mol.) was added in 15 min. Reaction took place immediately. The mixture was treated as described for the reaction with ethyl thiobenzoate and give toluene-*p*-sulphonamide, benzoic acid, barium sulphate, and *S*-2-diethylaminoethyl-*S*-toluene-*p*-sulphonamido-*N*-toluene-*p*-sulphonylsulphidimine.

The free base was unchanged after treatment with chloramine-T (2 mol.) for 20 hr.

*Reactions of Ethanesulphonic Acid and Related Compounds with Chloramine*-T.—Sodium ethanesulphonate (9·0 g.) (prepared by hydrolysis of ethanesulphonyl chloride), hydrochloric acid (5·43 g.; *d* 1·18), and chloramine-T (30·21 g.) in water (350 ml.) were boiled under reflux for 10 hr. Barium sulphate (0·62 g.), toluene-*p*-sulphonamide (13·60 g.), and unchanged sodium ethanesulphonate were isolated.

A similar reaction with ethanesulphonyl chloride (10·0 g.) gave sodium ethanesulphonate (11·15 g.) and barium sulphate (0·72 g.).

A solution of sodium ethanesulphinate (2·0 g.), hydrochloric acid (1·43 g.; *d* 1·18), and chloramine-T (4·02 g.) in 20% aqueous ethanol (110 ml.) was boiled under reflux for ¾ hr. Toluene-*p*-sulphonamide, (2·35 g.), m. p. and mixed m. p. 130°, sodium ethanesulphonate (1·38 g.), and barium sulphate (0·237 g.) were isolated.

*Reaction of Diethyl* N-*Toluene*-p-*sulphonylphosphoramidate with Chloramine*-T.—(a) *At* pH 2. The amidate (1·0 g.) and chloramine-T (0·90 g.) were dissolved in 30% aqueous ethanol (30 ml.). The solution was acidified with hydrochloric acid and boiled for 30 min., then basified with sodium carbonate solution and extracted continuously with ether (12 hr.). The extracts gave toluene-*p*-sulphonamide (0·56 g.), m. p. and mixed m. p. 137—138°. The aqueous layer was acidified and extracted with ether, giving an oil (1·0 g.) which slowly crystallised. Recrystallisation from dilute hydrochloric acid gave the unchanged amidate, m. p. and mixed m. p. 100°.

(b) *At* pH 10. A solution of the amidate (1·0 g.), sodium carbonate (0·34 g.), and

chloramine-T (0·90 g.) in 25% aqueous ethanol (40 ml.) was boiled for 6½ hr. Toluene-*p*-sulphonamide and the unchanged amidate (0·95 g.) were isolated.

*Kinetics of the Alkaline Hydrolysis of Triethyl Phosphorothiolate.*—The method described by Thain [23] was used. The following rate constants (l. mole$^{-1}$ sec.$^{-1}$, at 25°) were obtained: (*a*) Thiolate (1 g.) in 0·05N-KOH (250 ml.), $k_2 = 0·154$. (*b*) With added chloramine-T (5%), $k_2 = 0·158$. (*c*) With added chloramine-T (10%), $k_2 = 0·155$.

*Reaction of Triethyl Phosphorothionate with Chloramine-T.*—(a) 1 : 2 *Moles at* 25°. Chloramine-T (14·1 g.) in 30% aqueous ethanol (140 ml.) was added slowly to triethyl phosphorothionate (5·0 g.) in ethanol (30 ml.) and the mixture left at room temperature for 15 hr. The pale yellow solid which separated was collected, washed with light petroleum, and extracted with boiling water, leaving sulphur (0·11 g.), m. p. 114·5° (Found: S, 98·1%). The aqueous extracts yielded toluene-*p*-sulphonamide (7·0 g.), m. p. and mixed m. p. 137—138°. Ethanol was distilled from the filtrate and the residue, after basification with aqueous sodium carbonate, was extracted with chloroform. These extracts, combined with the light petroleum washings of the sulphonamide fraction, yielded an oily solid, which was washed with light petroleum, leaving toluene-*p*-sulphonamide (0·75 g.), m. p. 130°. The light petroleum washings were distilled, giving a fraction (3·15 g.), b. p. 108—114°/20 mm., $n_D^{25}$ 1·4209, which was identified by its infrared spectrum as a mixture of unchanged triethyl phosphorothionate and triethyl phosphate. This finding was confirmed by gas–liquid chromatography (2 m. column, packing "C", 194°, column pressure 0·6 kg. cm.$^{-2}$) which showed that the mixture contained 50% of triethyl phosphorothionate. The extracted reaction mixture, when acidified and treated with barium chloride, gave barium sulphate (1·903 g.).

(b) 1 : 4·7 *Moles at* 80°. Triethyl phosphorothionate (5·0 g.) and chloramine-T (26·29 g.) in 10% aqueous ethanol (350 ml.) were boiled under reflux for 2 hr. Toluene-*p*-sulphonamide (15·12 g.), sulphur (0·13 g.), barium sulphate (4·795 g.), and triethyl phosphate (2·16 g.), b. p. 100—101°/12 mm., $n_D^{25}$ 1·4030, were isolated, but no triethyl phosphorothionate was recovered.

*Reaction of Sulphur with Chloramine-T.*—Sulphur (0·64 g.) and chloramine-T (11·28 g.) in water (150 ml.) were boiled under reflux for 2 hr. Unchanged sulphur (0·28 g.) was separated from the hot reaction mixture, which was then allowed to cool. Toluene-*p*-sulphonamide (4·83 g.), m. p. and mixed m. p. 137—138°, was collected and the mother-liquors were extracted with chloroform to give more sulphonamide (1·35 g.), m. p. 132°. The aqueous layer, on treatment with barium chloride, gave barium sulphate (2·613 g.).

The authors' thanks are accorded to Dr. W. R. Foster who carried out the kinetic determinations and confirmed some of their observations, and to Dr. C. J. M. Stirling for helpful discussions.

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[23] Thain, *J.*, 1957, 4694.

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## 1082. *The Reactivity of Organophosphorus Compounds. Part IX.*[1] *The Reaction of Thionates with Alkyl Iodides.*

By A. J. BURN and J. I. G. CADOGAN.

The reaction, EtO·P(:S)XY + RI ⟶ RS·P(:O)XY + EtI, where X and Y are R, RO, RS, or $R_2N$, has been investigated. Kinetic measurements and qualitative experiments based on analyses of products have shown that the reaction proceeds most readily when X and Y are amino- or substituted amino-groups and, in all cases, is accelerated when conducted in solvents of high dielectric constant. The preparative consequences are discussed.

ALKYLATION of simple phosphorothionates was first reported by Emmett and Jones,[2] who noted that trimethyl phosphorothionate, $(MeO)_3PS$, on heing heated gave the isomeric

[1] Part VIII, Cadogan and Moulden, preceding paper.
[2] Emmett and Jones, *J.*, 1911, **99**, 713.

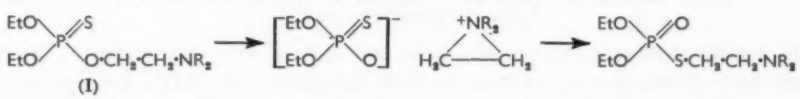
thiolate, $(MeO)_2PO{\cdot}SMe$. About the same time Pishchimuka [3] described the formation of *S*-butyl diethyl phosphorothiolate in the reaction of triethyl phosphorothionate with n-butyl iodide: $(EtO)_3PS + Bu^nI \longrightarrow (EtO)_2PO{\cdot}SBu^n + EtI$. Both reactions required vigorous conditions to ensure good conversions, and synthetic exploitation has been slight, although Kabachnik and his co-workers [4] recently demonstrated that dialkyl alkylphosphonothionates rearrange to the isomeric thiolates in the presence of the appropriate

$$(RO)_2PS{\cdot}R'' + R'Br \longrightarrow (RO)(R'S)PO{\cdot}R'' + RBr$$

alkyl halide at high temperatures. They restricted the reaction (i) to the case of $R = R'$. The common mechanism of these reactions is almost certainly of the type:

$$(RO)_2P{=}S \curvearrowright R'{-}X \curvearrowleft \longrightarrow [(RO)_2P{\cdot}SR']^+X^- \longrightarrow (RO)_2PO{\cdot}SR' + RX \quad . \quad . \quad . \quad . \quad (i)$$

where R'X is $(MeO)_3PS$ in the first case and $Bu^nI$ in the second. The reaction would, therefore, be expected to occur more readily with a highly electrophilic α-carbon atom in R'X and/or a highly nucleophilic sulphur atom in the phosphorothionate. Evidence concerning the first factor is available. It has been shown in this investigation and elsewhere [5] that triethyl phosphorothionate is much more slowly isomerised by heat to the corresponding thiolate than is the trimethyl analogue, in which the alkyl groups are more electrophilic. On the other hand, the isomerisation of 2-dialkylaminoethyl diethyl phosphorothionates (I) to the corresponding thiolates,[6] and that of the 2-ethylthioethyl analogue [7] to *S*-2-ethylthioethyl diethyl phosphorothiolate, occurs very readily.

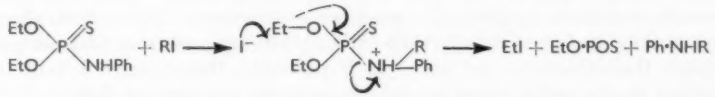


(I)

The driving force in these reactions is the ease of ionisation of these compounds which is a result of the stability of the intermediate ethyleniminium (or sulphonium) ions. The overall effect is therefore that of a thionate containing a highly electrophilic alkyl group.

Little is known of the factors which influence the nucleophilicity of the $\geq P{=}S$ group, and it was our intention, by a study of the effect of substituent groups in the phosphorothionate on the ease of its reaction with alkyl halides, to measure such factors.

The reaction of thionates with alkyl iodides has now been extended to phosphoroamidates (II), such as diethyl *N*-cyclohexylphosphoroamidothionate (II; X = EtO, $Y = NH{\cdot}C_6H_{11}$) and ethyl *NN'*-dicyclohexylphosphorodiamidothionate (II; $X = Y = NH{\cdot}C_6H_{11}$). In theory, amidothionates could react in two ways with alkyl iodides: at the sulphur atom as described in equation (i), and at the nitrogen atom, thus:

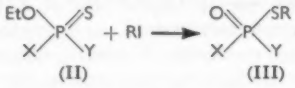


since it has been shown [8] that in certain circumstances the nitrogen atom of phosphoramidates is appreciably nucleophilic.

However, when an alkoxyl group (generally ethoxyl) was present in the thionate, *S*-alkyl compounds corresponding to the alkyl iodide used were obtained, and no evidence in favour of participation of the nitrogen atom in the reaction was found. The structures

[3] Pishchimuka, *J. Russ. Phys. Chem. Soc.*, 1912, **44**, 1406.
[4] Kabachnik, Mastryukova, and Kurochkin, *Bull. Acad. Sci. U.S.S.R.*, 1956, 185.
[5] Walling and Rabinowitz, *J. Amer. Chem. Soc.*, 1959, **81**, 1243.
[6] Fukoto and Stafford, *J. Amer. Chem. Soc.*, 1957, **79**, 6083; Tammelin, *Acta Chem. Scand.*, 1957, **11**, 1738.
[7] Fukoto and Metcalf, *J. Amer. Chem. Soc.*, 1954, **76**, 5103.
[8] Cadogan, *J.*, 1957, 1079.

of the resulting thiolates (III) were confirmed by analyses, infrared spectrography, and independent syntheses, in two cases, and in appropriate cases the presence of a P·SEt




(ii)

group in the product was confirmed by the formation of *S*-ethyl-*S*-toluene-*p*-sulphonamido-*N*-toluene-*p*-sulphonylsulphidimine [1] (IV).

Qualitative experiments indicated that the amidothionates reacted much more readily in reaction (ii) than did triethyl phosphorothionate under comparable conditions. More accurate kinetic experiments have confirmed this, as shown in Table 1, in which mean values are given for the constant obtained for reactions of propyl iodide with a series of thionates.

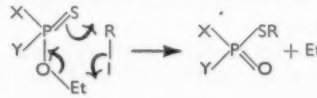
TABLE 1.

Reactions of thionates EtO·P(:S)XY with Pr$^n$I (10 mol.) at 105°.

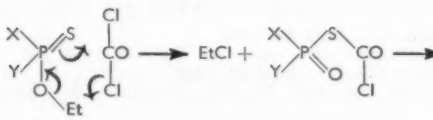
| X | Y | $t_{\frac{1}{2}}$ (hr.) | $10^5k$ (sec.$^{-1}$) * | X | Y | $t_{\frac{1}{2}}$ (hr.) | $10^5k$ (sec.$^{-1}$) * |
|---|---|---|---|---|---|---|---|
| NH·$C_6H_{11}$ | NH·$C_6H_{11}$ | 0·48 | 40 | EtO | Me | 23 | 0·85 |
| NH·$C_6H_4$Me-*p* | NH·$C_6H_4$Me-*p* | 2·6 | 7·5 | EtO | Ph | 32 | 0·60 |
| EtO | $NH_2$ | 3·5 | 5·5 | EtO | EtO | 43 | 0·45 |
| EtO | NH·$C_6H_{11}$ | 5·5 | 3·5 | EtO | EtS | 55 | 0·35 |
| EtO | Piperidino | 6·9 | 2·8 | EtO | Cl | *ca.* 15 days | — |
| EtO | NH·$C_6H_4$Me-*p* | 14 | 1·4 | | | | |

* Pseudounimolecular reaction.

The results show that the presence of groups such as $NH_2$, NHR, $NR_2$, and NHAr strongly facilitates the reaction of thionates with alkyl iodides, diamidates being particularly reactive. Within the limits of our experiments it can also be seen that thionates containing less powerful electron-donating groups such as methyl, ethoxyl, and thioethyl react less readily, while the chloridothionate, containing the strongly electron-attracting chlorine atom, is effectively unreactive. *OO*-Diethyl hydrogen thiophosphite $(EtO)_2PHS$, also reacted very slowly with propyl iodide, to give ethyl iodide, but in a non-first-order process, indicating that the basic reaction is different in this case. The order of activation of the process by substituent groups is therefore: $R_2N$, etc. > R > RO > RS. The lower reactivity of triethyl phosphorothionate than of diethyl methylphosphonothionate is interesting since it suggests greater electron repulsion by the methyl than by the ethoxyl group. A complete explanation of the differences in reactivity must await a more exhaustive kinetic analysis and would even then require a knowledge, so far unavailable, of the stereochemistry of the transition state in each case. The observed greater reactivity of the sulphur atom in phosphonothionates than in phosphorothionates is in accord with the only results concerning nucleophilic reactions of thionates. It has been shown [9] that the phosphonothionates react readily with carbonyl chloride, whereas phosphorothionates and phosphorothiolothionates do not. It is probable, therefore, that both types of reaction follow similar paths which can be schematically represented thus:




(iii)

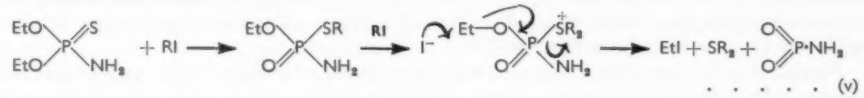



(iv)

[9] Cadogan, *J.*, 1961, 3067.

By analogy with the ease with which the reactions of amidothionates and alkyl iodides occur it is predicted that the reactions of the former with carbonyl chloride should also occur readily, but no relevant experimental evidence is available. Regardless of whether the conversion of thionates into thiolates proceeds as described in equation (i) or by a concerted process as outlined in equation (iii), the presence of alkyl groups more electrophilic than ethyl would probably facilitate the overall reaction. This view is supported by the observation that, in the reaction of benzyl diethyl phosphorothionate with propyl iodide, debenzylation occurs 2·5 times more readily than de-ethylation.

In the reactions of thionates with propyl iodide the first-order plot for the formation of ethyl iodide was linear over most of the reaction. In the case of diethyl phosphoramidothionate slight curvature of the plot corresponding to an increased rate of formation of the iodide was observed, suggesting that further reaction between newly formed thiolate and propyl iodide had occurred:




This is supported by the observation that ethyl *S*-propyl phosphoramidothioate (III; R = Pr$^n$, X = EtO, Y = $NH_2$) with propyl iodide gives ethyl iodide at a slow but significant rate ($k_1 = 4{\cdot}2 \times 10^{-6}$ sec.$^{-1}$; $t_{\frac{1}{2}} = 46$ hours), and by isolation from the reaction of diethyl phosphoramidothionate (II; X = EtO, Y = $NH_2$) and methyl iodide of a small quantity of trimethylsulphonium iodide, formed presumably from dimethyl sulphide [equation (v); R = Me]. Such a process would also account for Emmett and Jones's observation [2] that the reaction of trimethyl phosphorothiolate with methyl iodide gave trimethylsulphonium iodide.

TABLE 2.

Reaction of thionates with Pr$^n$I (10 mol.) in solvents (10 mol.).

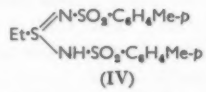
| Solvent | Dielectric constant | $(EtO)_2PS{\cdot}NH{\cdot}C_6H_{11}$ $t_{\frac{1}{2}}$ (hr.) | $(EtO)_2PS{\cdot}NH{\cdot}C_6H_{11}$ $10^5k$ (sec.$^{-1}$) | $(EtO)_2PPhS$ $t_{\frac{1}{2}}$ (hr.) | $(EtO)_2PPhS$ $10^5k$ (sec.$^{-1}$) |
|---|---|---|---|---|---|
| Pr$^n$I | 5 | 5·5 | 3·5 | 32 | 0·6 |
| $Me_2{\cdot}CH{\cdot}NO_2$ | 25 | 2·4 | 8·0 | 15 | 1·3 |
| $Ph{\cdot}NO_2$ | 33 | 2·2 | 8·6 | 14 | 1·4 |
| Me·CO·NHMe | 166 | 0·49 | 39·0 | 5·3 | 3·6 |

The use of solvents of increasing dielectric constant [nitromethane or 2-nitropropane ($\varepsilon = 25$), nitrobenzene (33), or *N*-methylacetamide (166) [10]] appreciably increased the rates of the reaction of thionate with propyl iodide without affecting the nature of the products (Table 2). The use of such solvents, particularly of nitromethane, which as a low-boiling liquid facilitates the isolation of the products, considerably enhances the usefulness of this route to compounds previously difficult to prepare. The formation of diethyl *S*-methyl phosphorothioate from methyl iodide and triethyl phosphorothionate for example, requires several weeks at the boiling point of the iodide, 5 days in the presence of nitromethane, and 45 minutes in the presence of *N*-methylacetamide at 105°. The use of the *N*-methylacetamide as a solvent also appreciably increased the rate of thermal isomerisation of triethyl phosphorothionate to thiolate, a process usually difficult to effect.[5]

*O*-Dealkylation occurs in all of the reactions discussed above. This, coupled with the high reactivity of diamides, suggested that phosphorothioic triamides and related compounds not containing alkoxyl groups should react readily with alkyl iodides to give

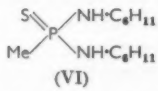
[10] Leader and Gormley, *J. Amer. Chem. Soc.*, 1951, **73**, 5731; Williams, Ellard, and Dawson, *ibid.*, 1957, **79**, 4652.

products of a type not isolable from similar reactions of phosphoramidothioic esters. In accord with this, hexa-*N*-ethylphosphorothioic triamide (V) and *NN'*-dicyclohexylmethylphosphonothioic diamide (VI) with methyl iodide readily gave stable crystalline monomethiodides.



(IV)

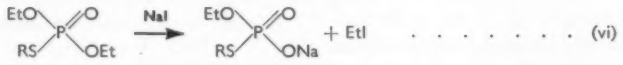
(V)



(VI)

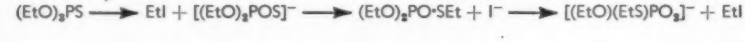
Although the exact structure of these adducts, which dissociate when heated *in vacuo*, has not been established, the methyl group is probably associated with the sulphur atom of the thionate, as in $[(Et_2N)_3P{\cdot}SMe]^+I^-$, since aqueous hydrolysis of the *NN'*-dicyclohexylmethylphosphonothioic diamide methiodide gives a strong odour of methanethiol. The triamide methiodide, when heated with triethylamine, gave triethylamine methiodide and hexa-*N*-ethylphosphorothioic triamide. Similar adducts of trimethylphosphine sulphide and methyl iodide have been described.[11]

Pertinent to the foregoing discussion are the reactions of sodium iodide with phosphorothioates. In agreement with the above observations *O*- rather than *S*-dealkylation of triethyl and *S*-benzyl diethyl phosphorothiolates by sodium iodide in ethyl methyl ketone readily occurs:



(vi)

In the case of triethyl phosphorothionate, however, sodium *OS*-diethyl phosphorothioate, rather than the expected *OO*-diethyl ester, was isolated. Plainly, in this case, *O*-dealkylation first occurs to give ethyl iodide and the bidentate *OO*-diethyl phosphorothioate ion, which further reacts by way of the more nucleophilic form, $(EtO)_2P(:O)S^-$, to give triethyl phosphorothiolate with the regeneration of sodium iodide. Reaction as in (vi) then gives the observed product.



## Experimental

Extracts were dried over magnesium sulphate. The light petroleum used had b. p. 40—60°. The infrared spectra in the region 2—15 μ were obtained by using a Perkin-Elmer model 21 double-beam spectrophotometer fitted with a rock-salt prism. Those in the region of 15—25 μ were recorded on a Hilger H.800 double-beam spectrophotometer fitted with a potassium bromide prism. Liquids were examined as capillary films between potassium bromide plates, and solids in potassium chloride or bromide discs. The provision of these facilities by Mr. L. C. Thomas, and his help in the interpretation of the spectra, which was in part based on his unpublished correlations, are gratefully acknowledged.

*Preparation of Compounds.*—Triethyl phosphorothionate and phosphorothiolate were prepared as described in Part VIII.[1] Diethyl methylphosphonothionate, b. p. 78°/10 mm., $n_D^{25}$ 1·4605, was prepared by the reaction of methylphosphonothioic dichloride with ethanolic sodium ethoxide (Found: C, 35·4; H, 7·8. Calc. for $C_5H_{13}O_2PS$: C, 35·7; H, 7·8%). Hoffmann, Wadsworth, and Weiss [12] reported b. p. 46°/2·3 mm., $n_D^{25}$ 1·4619. *Diethyl phenylphosphonothionate*, b. p. 163°/20 mm., 96°/0·05 mm., $n_D^{25}$ 1·5370, was similarly prepared (50%) from phenylphosphonothioic dichloride (Found: C, 52·6; H, 6·6. $C_{10}H_{15}O_2PS$ requires C, 52·2; H, 6·6%). *Benzyl diethyl phosphorothionate* was prepared by boiling diethyl phosphorochloridothionate (50 g.) in benzene (100 ml.) with a solution of sodium benzyloxide [formed from benzyl alcohol (32 g.) and sodium (6·9 g.)] in benzene (300 ml.) for 2 hr. Benzene (200 ml.) was removed by distillation, light petroleum (300 ml.) was added, and the mixture filtered

[11] Hantzsch and Hibbert, *Ber.*, 1907, **40**, 1508.
[12] Hoffmann, Wadsworth, and Weiss, *J. Amer. Chem. Soc.*, 1958, **80**, 3945.

through Celite 545. Distillation and redistillation gave a product (30 g.), b. p. 130°/0·2 mm., $n_D^{25}$ 1·5120 (Found: C, 50·9; H, 7·0. $C_{11}H_{15}O_3PS$ requires C, 50·75; H, 6·6%).

*OO*-Diethyl hydrogen phosphorothioite, b. p. 86°/20 mm., $n_D^{25}$ 1·4600 (Found: C, 32·0; H, 7·3. Calc. for $C_4H_{11}O_2PS$: C, 31·2; H, 7·2%), was prepared (46%) by the method of Krawiecki and Michalski [13] who reported b. p. 75—76°/14 mm., $n_D^{20}$ 1·4608. *OOS*-Triethylphosphorodithioate, b. p. 127°/15 mm., $n_D^{25}$ 1·5019, was prepared (70%) by reaction of potassium *OO*-diethyl phosphorodithioate [14] with methanolic ethyl bromide.

Ethyl *P*-methyl-*N*-phenylphosphonamidothionate was prepared as follows: Dry ($MgSO_4$) triethylamine (6·8 g.) in ethanol (3·1 g.) and dry (Na) benzene (30 ml.) was added dropwise to methylphosphonothioic dichloride (10 g.) in dry benzene (80 ml.), and the mixture was boiled under reflux for 6 hr. On the next day, after filtration, the solution was washed with water (3 × 50 ml.) and dried. Distillation of the solution gave ethyl methylphosphonochloridothionate (7·2 g., b. p. 103°/70 mm., $n_D^{25}$ 1·4930. Hoffmann, Wadsworth, and Weiss [13] reported b. p. 41°/4·0 mm., $n_D^{25}$ 1·4950. A mixture of aniline (4·1 g.) and triethylamine (4·5 g.) in dry benzene (30 ml.) was added to the foregoing chloridate (7·2 g.) in benzene (80 ml.). After 3 hr. at the b. p. the mixture was filtered, was washed with water (3 × 50 ml.), and dried. Distillation gave *ethyl* P-*methyl*-N-*phenylphosphonamidothionate* (7·25 g.), b. p. 125°/0·05 mm., $n_D^{25}$ 1·5770 (Found: C, 49·5; H, 6·5. $C_9H_{14}NOPS$ requires C, 50·2; H, 6·6%).

*OS*-Diethyl *N*-cyclohexylphosphoramidothioate was prepared by the addition of ethanethiol (20·8 g.) in ether (Na-dry; 50 ml.) to ethyl phosphorodichloridate (54·3 g.) and triethylamine (33·8 g.) in dry ether (300 ml.), followed by boiling for 2 hr.; cyclohexylamine (67 g., 2 mol.) was then added in dry ether (100 ml.). After a further 2 hr. at the b. p. the mixture was filtered, washed with water (2 × 100 ml.), and dried. Distillation gave a poor yield (19%) of material of b. p. 140°/0·25 mm., m. p. 53—54°.

Amidates derived from diethyl phosphorochloridothionate were prepared by reaction of the appropriate amine (2 mol.) with the chloridothionate (1 mol.) in a suitable boiling solvent, followed by washing and purification. *Diethyl* N-*cyclohexylphosphoramidothionate*, prepared (52%) in ether (2 hr.), had b. p. 121°/0·75 mm., $n_D^{25}$ 1·4920 (Found: C, 47·6; H, 8·9. $C_{10}H_{22}NO_2PS$ requires C, 47·8; H, 8·8%). *Diethyl* N-p-*tolylphosphoramidothionate*, prepared (40%) in toluene (17 hr.), had m. p. 38° (from light petroleum) (Found: C, 51·0; H, 6·5. $C_{11}H_{18}NO_2PS$ requires C, 51·0; H, 7·0%). Diethyl phosphoramidothionate, prepared (87%) by passing ammonia through an ether solution of the chloridate for 4 hr., had b. p. 132°/20 mm., $n_D^{26.5}$ 1·4842 (Found: C, 28·5; H, 7·4. Calc. for $C_4H_{12}NO_2PS$: C, 28·4; H, 7·2%). Mel'nikov and Zen'kevich [15] reported b. p. 112—115°/9 mm., $n_D^{20}$ 1·4828. *Ethyl* NN′-*dicyclohexylphosphorodiamidothionate*, prepared (53%) from ethyl phosphorodichloridothionate [16] (1 mol.) and cyclohexylamine (4 mol.) in ether at room temperature, had m. p. 76° (from aqueous ethanol) (Found: C, 55·7; H, 9·7. $C_{14}H_{29}N_2OPS$ requires C, 55·3; H, 9·6%). *Ethyl* NN′-*di*-p-*tolylphosphorodiamidothionate*, which could not be prepared by the previous method, was obtained as follows: Ethyl phosphorodichloridite (11·8 g.) in dry ether (100 ml.) was added dropwise to *p*-toluidine (34·4 g.) in dry ether (300 ml.). After removal of the hydrochloride by filtration, sulphur (2·6 g.) was added in small portions. Removal of the solvent at 40 mm. left a viscous liquid which, on treatment with boiling ethanol, deposited sulphur (0·4 g.), which was collected. After 7 days at 0° crystals (6%), m. p. 107°, were deposited (Found: C, 60·2; H, 6·6. $C_{16}H_{21}N_2OPS$ requires C, 60·0; H, 6·6%).

NN′-*Dicyclohexylmethylphosphonothioic diamide*, obtained in 53% yield from methylphosphonothioic dichloride (1 mol.) and cyclohexylamine (4 mol.), had m. p. 115° after recrystallisation from benzene–light petroleum (Found: C, 56·9; H, 9·6. $C_{13}H_{27}N_2PS$ requires C, 56·9; H, 9·9%).

*Hexa-N-ethylphosphorothioic Triamide.*—Phosphorus trichloride (34·4 g.) in dry ether (100 ml.) was added dropwise to an ice-cooled solution of diethylamine (146 g.) in ether (300 ml.). The reaction was extremely vigorous. After 3 hr. the hydrochloride was removed and the filtrate was evaporated under reduced pressure. Sulphur (8 g.) was added portionwise (0·25 g.) at <25° to the residue in light petroleum (200 ml.). The resulting solution was filtered through Celite 545 and evaporated under reduced pressure to leave a red liquid (61·5 g.). Distillation

[13] Krawiecki and Michalski, *J.*, 1960, 881.
[14] Cadogan and Thomas, *J.*, 1960, 2248.
[15] Mel'nikov and Zen'kevich, *J. Gen. Chem. U.S.S.R.*, 1955, **25**, 793.
[16] *Inorg. Synth.*, 1953, **4**, 75.

of the product, which occurred with much charring, gave the triamide as a pale red oil (48%), b. p. 104°/0·025 mm., $n_D^{22.5}$ 1·5040 (lit.,[17] b. p. 120—121°/0·1 mm., $n_D^{20}$ 1·5052) (Found: C, 51·5; H, 11·3. Calc. for $C_{12}H_{30}N_3PS$: C, 51·6; H, 10·8%).

*Reactions of Thionates with Alkyl Iodides.*—(i) *Isolation of products.* (*a*) The reactions were effected by boiling a mixture of the thionate (1 mol.) and alkyl iodide (5—10 mol.) until reaction was complete, as shown by the appearance of P=O absorption in the infrared spectrum. The corresponding *S*-alkyl compound was isolated by distillation alone and/or recrystallisation as necessary. The method is exemplified by the reaction of methyl iodide with diethyl phosphoramidothionate: The amidate (4·9 g.) and methyl iodide (18·2 g.) were boiled under reflux for 4¼ hr. When cool, the colourless crystals which had been deposited were collected and washed with methyl iodide (3 ml.). Crystallisation from benzene gave trimethylsulphonium iodide (0·1 g.), m. p. and mixed m. p. 202—206° (correct infrared spectrum). Light petroleum was added to the mother liquors to precipitate O-*ethyl* S-*methyl phosphoramidothiolate*, which on recrystallisation from benzene–light petroleum had m. p. 67·5° (4 g., 89%) (Found: C, 23·4; H, 6·1. $C_3H_{10}NO_2PS$ requires C, 23·2; H, 6·5%).

Similar reactions are summarised in Table 3.

TABLE 3.

Details of the reaction EtO·P(:S)XY + RI ⟶ RS·P(:O)XY + EtI.

| | | | | | Properties of RS·P(:O)XY | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | R in | Time | Yield | | | Found (%) | | | Reqd. (%) |
| X | Y | RI | (hr.) | (%) | M. p. | B. p./mm. | C | H * | Formula | C H |
| EtO | $NH_2$ | Et | 22 | 66 | 51° [1] | — | 28·4 | 7·1 | $C_4H_{12}NO_2PS$ | 28·4 7·1 |
| EtO | $NH_2$ | Pr$^n$ | 18 | 55 | — | 122—128°/0·05 [a] | 33·0 | 7·6 | $C_5H_{14}NO_2PS$ | 32·8 7·7 |
| EtO | NH·$C_6H_{11}$ | Et | 22 | 83 | 61 | 130°/0·25 | 47·9 | 8·7 | $C_{10}H_{22}NO_2PS$ | 47·8 8·8 |
| EtO | NH·$C_6H_{11}$ | Pr$^n$ | 19 | 98 | 30—32 | — | 49·6 | 8·9 | $C_{11}H_{24}NO_2PS$ | 49·8 9·1 |
| EtO | NH·$C_6H_4$Me-*p* | Me | 23 | 98 | 88·5—91·5 | — | 49·3 | 6·9 | $C_{10}H_{16}NO_2PS$ | 49·0 6·6 |
| EtO | NH·$C_6H_4$Me-*p* | Et | 36 | 86 | 59—61 | 137—140°/0·025 | 51·0 | 7·0 | $C_{11}H_{18}NO_2PS$ | 51·0 7·0 |
| NH·$C_6H_{11}$ | NH·$C_6H_{11}$ | Pr$^n$ | 3 | 91 | 158 [1] | — | 56·2 | 9·8 | $C_{15}H_{31}N_2OPS$ | 56·6 9·8 |
| NH·$C_6H_4$Me-*p* | NH·$C_6H_4$Me-*p* | Pr$^n$ | 12 | 90 | 161 [2] | — | 61·3 | 6·6 | $C_{17}H_{23}N_2OPS$ | 61·1 6·9 |
| EtO | Me | Pr$^n$ | 92 | 51 | — | 106°/10 [b] | 39·7 | 8·6 | $C_6H_{15}O_3PS$ | 39·6 8·3 |
| EtO | Ph | Pr$^n$ | 8 days | 78 | — | 116°/0·01 [c] | 54·3 | 7·0 | $C_{11}H_{17}O_3PS$ | 54·1 7·0 |
| NH·$C_6H_{11}$ | NH·$C_6H_{11}$ | Me | 24 [3] | 71 | 175 | — | 54·1 | 9·1 | $C_{13}H_{27}N_2OPS$ | 53·8 9·4 |
| EtO | Piperidino | Pr$^n$ | 41·5 | 66 | — | 106—110°/0·05 [d] | 48·2 | 8·8 | $C_{10}H_{22}NO_2PS$ | 47·8 8·8 |

* Recryst. from (1) benzene–light petroleum, (2) aq. EtOH. [3] Reaction at room temperature. $n_D^{25}$ (*a*) 1·4906, (*b*) 1·4718, (*c*) 1·5365, (*d*) 1·4919.

(*b*) For reactions carried out in solvents, in general, an excess (10—20 mol.) of an equimolar mixture of alkyl iodide and nitromethane or *N*-methylacetamide was used. Ethyl *p*-methyl-*N*-phenylphosphonamidothionate (2·15 g.), for example, ethyl iodide (8·2 g., 5 mol.), and nitromethane (3·1 g., 5 mol.) were boiled under reflux for 18 hr. Removal of the solvents left *S*-ethyl *P*-methyl-*N*-phenylphosphonamidothioate, which on recrystallisation from benzene–methanol (trace) had m. p. 155° (72%). Triethyl phosphorothionate (5 g., 1 mol.) on reaction with methyl iodide (35 g., 10 mol.) in nitromethane (15 g., 10 mol.) was similarly converted into *diethyl* S-*methyl phosphorothiolate* (3 g., 65%) b. p. 106°/8 mm., $n_D^{23}$ 1·4557 (Found: C, 33·0; H, 7·2. $C_5H_{13}O_3PS$ requires C, 32·6; H, 7·1%).

Experiments carried out in *N*-methylacetamide are exemplified by the following: Ethyl *NN'*-dicyclohexylphosphorodiamidothionate (1·0 g.), propyl iodide (6 g.), and *N*-methylacetamide (2·5 g.) were heated on a steam bath for 20 min. Water (50 ml.) was added and the product was extracted into 1 : 1 chloroform–benzene (2 × 125 ml.). The dried extracts were evaporated to 50 ml. and light petroleum (150 ml.) was added. The crystals (82%) of *S*-propyl *NN'*-dicyclohexylphosphorodiamidothioate which were precipitated had m. p. 158°, undepressed on admixture with a specimen prepared in the absence of *N*-methylacetamide.

[17] Stuebe and Lankelma, *J. Amer. Chem. Soc.*, 1956, **78**, 976.

The results of similar experiments with other thionates are summarised in Table 4. The physical constants of the products were identical with those obtained as described in Table 3.

(ii) *Structures.* The structures of the thiolates formed in the above reactions were further confirmed by examination of the relevant infrared spectra, when the presence of P–S–C (1258—1271 cm.$^{-1}$) [12] and P=O (8·15 μ) and absence of P=S (12·05 μ) were established in each case. The m. p. of *OS*-diethyl *N*-cyclohexylphosphoramidothiolate, prepared as described in Table 3, was undepressed on admixture with a sample prepared from ethyl phosphorodichloridate as described above, as was that of *S*-ethyl *P*-methyl-*N*-phenylphosphonamidothiolate on admixture with an authentic sample prepared by Cadogan's method.[9] The presence of the P·SEt group in *OS*-diethyl phosphoramidothioate was confirmed as follows: A solution of chloramine-T (6·2 g., 2 mol.) in 3 : 7 aqueous ethanol (30 ml.) was added portionwise (5 ml.) to *OS*-diethyl phosphoramidothioate (2 g., 1 mol.) in 3 : 7 aqueous ethanol (30 ml.). A colourless solid was at once precipitated and, after 2 hr. at 20°, was collected and washed with ethanol and light petroleum. Recrystallisation from ethanol gave *S*-ethyl-*S*-toluene-*p*-sulphonamido-*N*-toluene-*p*-sulphonylsulphidimine, m. p. 195° (decomp.) (1·7 g., 40%) undepressed on admixture with a specimen prepared as described by Cadogan and Moulden.[1] *OS*-Diethyl *N*-cyclohexylphosphoramidothioate similarly gave *S*-ethyl-*S*-toluene-*p*-sulphonamido-*N*-toluene-*p*-sulphonylsulphidimine, m. p. and mixed m. p. 193·5°.

TABLE 4.

Reactions of thionates, EtO·P(:S)XY with alkyl iodides in the presence of solvents at the b. p.

| X | Y | Solvent | R in RI | Time (hr.) | Yield (%) of RS·P(:O)XY |
|---|---|---|---|---|---|
| EtO | $NH_2$ | $MeNO_2$ | Et | 10 | 72 |
| EtO | NH·$C_6H_{11}$ | $MeNO_2$ | Et | 14 | 80 |
| EtO | NH·$C_6H_{11}$ | Me·CO·NHMe | Et | 2·5 | 52 |
| NH·$C_6H_{11}$ | NH·$C_6H_{11}$ | $MeNO_2$ | $Pr^n$ | 1·25 | 86 |
| NH·$C_6H_{11}$ | NH·$C_6H_{11}$ | Me·CO·NHMe | $Pr^n$ | 0·3 [1] | 82 |
| EtO | EtO | Me·CO·NHMe | Me | 0·75 [2] | 68 |
| EtO | EtO | $MeNO_2$ | Me | 120 | 65 |
| EtO | Me | Me·CO·NHMe | $Pr^n$ | 22 | 30 |
| EtO | Me | $MeNO_2$ | $Pr^n$ | 42·5 | 84 |
| EtO | Ph | $MeNO_2$ | $Pr^n$ | 96 | 80 |
| EtO | Piperidino | $MeNO_2$ | $Pr^n$ | 19 | 90 |
| Me | NHPh | $MeNO_2$ | Et | 18 | 72 |

[1] At 100°. [2] At 105°.

(iii) *Kinetic measurements.* The following reaction was studied: thionate + $Pr^nI$ ⟶ thiolate + EtI. In the presence of a ten-fold excess of $Pr^nI$ this was of the first order in thionate. The rate of formation of ethyl iodide was measured by gas–liquid chromatography.

Measurements were made with a Perkin-Elmer "Fraktometer" model 116, fitted with a high-sensitivity dual thermal conductivity detector. All injections were made using a precision liquid sample introduction system in which a current of nitrogen carrier gas by-passed from the main supply discharged the sample from a pipette into the injection block. Only one pipette (20 μl.) was used; it was filled by capillary action. A 2-m. column packed with silicone oil (DC.200) on Celite was used; it was used at 89° with a nitrogen flow of 18 ml./min. in early experiments and at 96° with a flow of 10 ml./min. in later experiments. The relative retention times under these conditions were $Pr^nI$ 1·5, EtI 1·0. Calibrations appropriate to the conditions and compounds used were made frequently, with solutions of ethyl iodide in propyl iodide in the range 0—9 mole % and ethyl iodide, in equimolar mixtures of propyl iodide and added solvent, in the range 0—5 mole %. In all cases a plot of ethyl iodide peak height against concentration was linear. By the use of such calibrations the concentrations of ethyl iodide and propyl iodide present in reaction mixtures were readily determined without tedious measurement of the areas of the relevant peaks on the chromatogram. Preliminary experiments were also performed to ensure that the sensitivity of the response did not vary appreciably with the bridge voltage of the detector.

In the kinetic experiments the reaction mixtures used were in the range 8—9 mole % for thionates in pure propyl iodide, and 4·4—4·6 mole % when added solvents were used in equimolar proportions to the propyl iodide. Eight samples (*ca.* 1 ml. each) of the mixture were then sealed into tubes (9 × 30 cm.), being placed at the bottom of the tube by use of a long pipette and cooled in ice–salt; the tubes were then quickly sealed. These samples were kept in a thermostat at 105° for appropriate times and cooled in ice. Injections of this ice-cold mixture were made until consistency was obtained, usually within 5%, 3—5 injections being taken. The propyl iodide was effectively constant in concentration and was therefore used as an internal normalisation standard. The results were calculated on the basis of $\ln (P_0/P) = kt$, where $P_0$ = initial concentration of thionate, and $P$ = concentration of thionate at time $t$.

The concentration of ethyl iodide was obtained from the peak height recorded on the chromatogram after correction, by means of the calibration graph. This concentration is effectively the same as that of thionate consumed.

In theory, ethyl iodide formed in this process can react with unchanged thionate, to give the corresponding ethyl thiolate and more ethyl iodide (equation ii). This reaction, which would escape detection by our analysis, is very unlikely at the concentrations used and is excluded by the product analyses described (Tables 3 and 4).

The results, which in each case are mean values obtained from several experiments, are summarised in Tables 1 and 2. A typical experiment is described in Table 5.

TABLE 5.

Reaction at 105° of PrI with $(EtO)_2P(:S)\cdot NH\cdot C_6H_{11}$ (8·75 molar %).

| $t$ (hr.) | 0 | 0·25 | 1·25 | 2·25 | 3·25 | 4·25 | 5·4 |
|---|---|---|---|---|---|---|---|
| EtI peak height ..... | 0 | 2·2 | 8·6 | 15·2 | 20·9 | 24·9 | 29·8 |
| [EtI], molar % ..... | 0 | 0·3 | 1·25 | 2·25 | 3·1 | 3·7 | 4·45 |
| [P = S] ,, ..... | 8·75 | 8·45 | 7·5 | 6·5 | 5·65 | 5·05 | 4·3 |

(iv) *Reaction of benzyl diethyl phosphorothionate with propyl iodide.* The thionate (1 g.) and propyl iodide (3·25 g., 5 mol.) were heated in a sealed tube at 105° for 20 hr. Gas–liquid chromatography (2-m. "C" column, 102°, rate of flow 14 ml./min.) revealed ethyl iodide (1·3% of propyl iodide present). Analyses at 170° indicated the presence of benzyl iodide (3% of propyl iodide present) and diethyl *S*-*n*-propyl phosphorothiolate. Hence the ratio of debenzylation to de-ethylation is 5 : 2.

(v) *Reaction of ethyl* S-*propyl phosphoroamidothiolate with propyl iodide.* The experiment was followed kinetically as described above, with a 10 molar excess of propyl iodide at 105°. Under these conditions the reaction was of the first order in ethyl iodide. The rate constant in pure propyl iodide was $4·2 \times 10^{-6}$ sec.$^{-1}$ ($t_{\frac{1}{2}}$ = 46 hr.) and in equimolar propyl iodide-*N*-methylacetamide, $k = 1·8 \times 10^{-5}$ sec.$^{-1}$ ($t_{\frac{1}{2}}$ = 11 hr.).

*Reaction of Hexa-*N*-ethylphosphorothioic Triamide with Methyl Iodide.*—The triamide (2·79 g.) and methyl iodide (1·42 g.) were kept at room temperature for 17 hr. The pale yellow crystalline product was triturated with ether and then boiled with ether for 3 hr. and filtered, to give the *triamide methiodide* as a white powder, m. p. 82° (Found: C, 37·0; H, 7·6. $C_{13}H_{33}IN_3PS$ requires C, 37·0; H, 7·9%). The adduct was stable at 50°/0·05 mm. for 3½ hr. but a portion (0·31 g.) after 1½ hr. at 77°/0·05 mm. gave hexa-*N*-ethylphosphorothioic triamide (0·18 g., 89%; $n_D^{25}$ 1·5036). A portion (1·0 g.) of adduct was boiled under reflux with triethylamine (5·0 g.) for 4 hr. Light petroleum (50 ml.) was added and the mixture was left overnight. The colourless solid (0·54 g., 95%) formed was collected and had m. p. 299° and mixed m. p. 301° with triethyl methyl ammonium iodide (m. p. 303°). The filtrate on distillation gave hexa-*N*-ethylphosphorothioic triamide (0·56 g., 86%; $n_D^{23}$ 1·5037; correct infrared spectrum).

*Reaction of* NN′-*Dicyclohexylmethylphosphonothioic Diamide with Methyl Iodide.*—The diamide (2·0 g.) and methyl iodide (5·0 g.) were kept at room temperature for 5 days. Removal of excess of methyl iodide, followed by treatment with ether as described in the previous experiment, gave *methyl* NN′-*dicyclohexylmethylphosphonothioic diamide methiodide* (2·1 g., 66%), m. p. 94—95° (Found: C, 40·9; H, 7·8. $C_{14}H_{30}IN_2PS$ requires C, 40·4; H, 7·3%). The adduct was completely converted into *NN*′-dicyclohexylmethylphosphonothioic diamide, m. p. and mixed m. p. 113° after 210 min. at 108°/0·1 mm., and after 6½ hr. at 84°/0·05 mm. A portion (0·62 g.) of the adduct was boiled under reflux in water (20 ml.) for 8 hr. The solution had pH

5—6. Methanethiol was evolved and removal of water left an unidentified solid which crystallised from ether–ethanol (0·17 g.; m. p. 194—196°) (Found: C, 43·5; H, 9·2%).

*Isomerisation of Triethyl Phosphorothionate in* N-*Methylacetamide*.—The thionate (1·0 g., 1 mol.) and *N*-methylacetamide (0·73 g., 2 mol.) were kept at 105° for 88 hr. Gas–liquid chromatography on a 2-m. "C" column at 190° with a flow rate of 12 ml./min. indicated that 16% of the thionate had isomerised to triethyl phosphorothiolate. The retention times relative to *N*-methylacetamide were $(EtO)_3PS$ 2·33, and $(EtO)_3PO{\cdot}SEt$ 3·56.

*Reactions of Sodium Iodide with Phosphorothiolates*.—(i) *With triethyl phosphorothiolate*. The ester (15 g.) and sodium iodide (11·4 g.) were boiled under reflux in ethyl methyl ketone (200 ml.) for 2 hr. The colourless needles (8·0 g.) which separated on cooling were washed with acetone and recrystallised from ethyl methyl ketone–acetone, to give *sodium* OS-*diethyl phosphorothiolate* in needles, m. p. 214° (Found: C, 25·6; H, 5·55. $C_4H_{10}NaO_3PS$ requires C, 25·0; H, 5·2%). The infrared spectrum exhibited bands attributable to $PO_2^-$ and $EtS{\cdot}PO_2^-$ (1258—1271 cm.$^{-1}$).[12] The structure of the product was confirmed by its conversion into the 1,1,4,4-tetra-ethylpiperazinium derivative as follows: the sodium salt (2 mol.) in a small volume of hot methanol was added to 1,1,4,4-tetraethylpiperazinium dichloride [13] (1 mol.) in hot methanol. The cooled mixture was filtered, evaporated to a small volume, and diluted with acetone. Crystallisation from this mixture of solvents gave 1,1,4,4-tetraethylpiperazinium bis-(*OS*-diethyl phosphorothiolate) as needles (75%), m. p. 203° (after drying over $P_2O_5$ at 50°/0·01 mm. for 12 hr.), undepressed on admixture with an authentic specimen prepared as described by Cadogan and Thomas.[14]

(ii) *With triethyl phosphorothionate*. The ester (5 g.) and sodium iodide (4 g.) were boiled under reflux in ethyl methyl ketone (90 ml.) for 6½ hr. The crystals (0·5 g.) which separated on cooling recrystallised from ethyl methyl ketone–acetone, to give sodium *OS*-diethyl phosphorothiolate, m. p. and mixed m. p. 212—214° (correct infrared spectrum).

(iii) *With* S-*benzyl diethyl phosphorothioate*. The ester (2·3 g.) and sodium iodide (1·3 g.) in ethyl methyl ketone (30 ml.) similarly gave, after 1½ hr., a salt (0·8 g.), m. p. 200°, which was identified as sodium *S*-benzyl ethyl phosphorothioate by conversion, as described above, into 1,1,4,4-*tetraethylpiperazinium bis*-(S-*benzyl ethyl phosphorothiolate*) which, crystallised in colourless needles from acetone–methanol (trace), had m. p. 112° (after drying over $P_2O_5$ at 40°/0·01 mm. for 1 hr.), undepressed on admixture with an authentic specimen prepared as described below (Found: C, 54·3; H, 7·9. $C_{30}H_{52}N_2O_4P_2S_2$ requires C, 53·8; H, 7·8%).

*SS*-Dibenzyl ethyl phosphorodithiolate was first prepared as a viscous oil from toluene-α-thiol and ethyl phosphorodichloridate in the presence of triethylamine, as described by Cadogan and Thomas [14] for the preparation of *OSS*-triethyl phosphorodithiolate. The ester (6·9 g.) was then hydrolysed by shaking it with sodium hydroxide (2·8 g.) in water (50 ml.) and dioxan (20 ml.) for 2 hr. The mixture was extracted with ether and the pH of the aqueous portion was adjusted to 7. 1,1,4,4-Tetraethylpiperazinium dichloride (2·7 g.) was added and the solution was evaporated to dryness at 20 mm. The residue was extracted with boiling methanol (2 × 100 ml.), and the filtrate was evaporated to a small volume and diluted with acetone. Crystallisation from this mixture of solvents gave 1,1,4,4-tetraethylpiperazinium bis-(*S*-benzyl ethyl phosphorothiolate), m. p. 112°.

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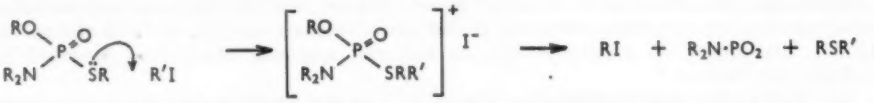
[12] Cadogan, *J.*, 1955, 2971.

## 1083. *The Reactivity of Organophosphorus Compounds. Part X.*[1] *The Reaction of Phosphorothiolates with Alkyl Iodides.*

By A. J. Burn, J. I. G. Cadogan, and H. N. Moulden.

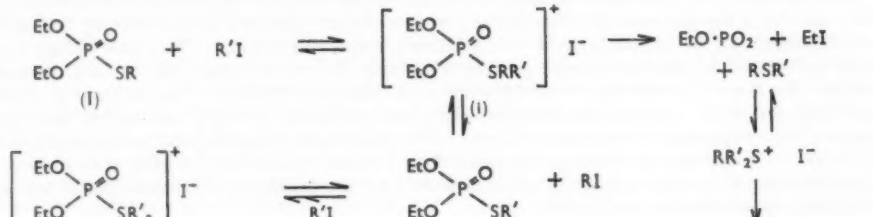
In Part IX of this series,[1] the reactivities of selected phosphoro- and phosphono-thionates toward alkyl iodides in the following reaction were reported:

The reaction was followed kinetically by measuring the rate of formation of the alkyl iodide (RI). In some cases there was evidence for the production of a small amount of alkyl iodide by an additional mechanism probably involving attack by the thiolate sulphur atom of the product on the alkyl halide (R'I):



Many years previously Emmett and Jones [2] reported the formation of trimethylsulphonium iodide in the reaction of methyl iodide with trimethyl phosphorothiolate $(MeO)_2P(:O)\cdot SMe$, a reaction also suggestive of nucleophilic attack by the thiolate sulphur atom on methyl iodide.

These observations are of interest because they suggest localisation of electrons on the sulphur atom in phosphorothiolates despite the conjugative proximity of the $\geqslant P{=}O$ group The possibility is also raised of the exchange of alkyl groups attached to the sulphur atom in phosphorothiolates by suitable choice of reagents. We therefore studied further the reactions of phosphorothiolates with alkyl iodides.



*S*-Benzyl diethyl phosphorothiolate (I; R = $Ph\cdot CH_2$) and methyl iodide, after prolonged heating, gave in addition to starting material, ethyl iodide, benzyl iodide, and trimethylsulphonium iodide. The presence of diethyl *S*-methyl phosphorothiolate (I; R = Me) was inferred but could not be confirmed because its mixture with benzyl iodide could not be satisfactorily resolved by gas–liquid chromatography. However, a similar reaction with ethyl iodide instead of methyl iodide indicated that alkyl group exchange had occurred since the products included ethyl iodide, benzyl iodide, and triethyl phosphorothiolate (I; R = Et). Diethyl *S*-methyl phosphorothiolate (I; R = Me) reacted similarly with ethyl iodide to give triethyl phosphorothiolate and methyl iodide.

[1] Part IX, Burn and Cadogan, *J.*, 1961, preceding paper.
[2] Emmett and Jones, *J.*, 1911, **99**, 713.

The formation of these products can be explained on the basis of the annexed series of reactions. The extent to which each occurs depends on many factors, the most important being the electrophilicity of the α-carbon atom of the alkyl halide; for example, ethyl bromide did not react with thiolates under the standard conditions.

These observations show that the thiolate sulphur atom in phosphorothiolates is appreciably nucleophilic, suggesting that delocalisation of the sulphur lone pair of electrons with the phosphoryl group is not strongly developed. That delocalisation of the nitrogen lone pair of electrons of related phosphoramidates is also similarly reduced has been demonstrated previously.[3]

*Experimental.*—Gas–liquid chromatography was carried out with a Perkin-Elmer "Fraktometer," model 116, fitted with a high-sensitivity dual thermal-conductivity detector. The response was tested by analysis of mixtures of known composition and found to be satisfactory. The columns, 2 m. in length, consisted of a silicone oil (DC 200) on Celite (C) or di-n-decyl phthalate on Celite (A).

*Preparation of compounds.* Triethyl phosphorothiolate (b. p. 95°/12 mm., $n_D^{25}$ 1·4553) and *S*-benzyl diethyl phosphorothiolate (b. p. 130°/0·2 mm., $n_D^{25}$ 1·5234) were prepared as described by Cadogan and Moulden,[4] and diethyl *S*-methyl phosphorothiolate (b. p. 106°/8 mm., $n_D^{25}$ 1·4547) as described in Part IX.[1]

*Reaction of diethyl* S*-methyl phosphorothiolate with ethyl iodide.* The thiolate (0·5 g.) and ethyl iodide (4·25 g., 10 mol.) were heated at 105° in a sealed tube for 47 hr. to give a clear liquid containing *ca.* 2% of an immiscible gum. The supernatant liquid was analysed by gas–liquid chromatography as follows:

(*a*) With a column temperature of 100°, packing C, and a flow of nitrogen of 12 ml./min., methyl iodide (1·2% of total iodide fraction) was detected in addition to ethyl iodide (relative retention times 1 : 1·2), indicating a 12% conversion of the *S*-methyl into *S*-ethyl thiolate on the assumption that reaction (i) is the only mode of formation of methyl iodide.

(*b*) With a column temperature of 170°, packing C, and a flow of nitrogen of 10 ml./min., triethyl phosphorothiolate (2% of total ester fraction) was detected in addition to diethyl *S*-methyl phosphorothiolate (relative retention times 1·33 : 1).

A similar experiment carried out at 105° for 130 hr. gave more of the unidentified gum (probably a sulphonium salt mixture). Analysis of the supernatant liquid indicated an increase in the amounts of methyl iodide (2·7% of total iodide, *i.e.*, 27% conversion based on reaction i) and of triethyl phosphorothiolate (3·4% of total ester).

*Reactions of* S*-benzyl diethyl phosphorothiolate.* (i) With methyl iodide. The thiolate (1·5 g.) and methyl iodide (4·1 g., 5 mol.) were heated at 105° for 6 hr. to give a dark red liquid containing crystals which were removed. The filtrate was analysed by gas–liquid chromatography under the conditions (*a*) and (*b*) described above, and shown to contain ethyl and methyl iodide (the former representing 0·25 mole/mole of thiolate) and a component having the same retention time as both benzyl iodide and diethyl *S*-methyl phosphorothiolate (*ca.* 0·1 mole/mole of *S*-benzyl thiolate). The presence of benzyl iodide was confirmed by conversion into benzyltriethylammonium iodide as described below.

A similar experiment was carried out at 100° (65 hr.) with thiolate (5·0 g.). The crystals were removed, and recrystallised from methanol, to give trimethylsulphonium iodide (1·01 g.), m. p. and mixed m. p. 209—210° (Found: C, 18·3; H, 4·6. Calc. for $C_3H_9IS$: C, 17·7; H, 4·4%). The mother liquors from the crystallisation gave an oil whose infrared spectrum showed the presence of more trimethylsulphonium iodide and inorganic phosphate. The filtrate from the original filtration was distilled to give the following fractions: (α) b. p. 40—58° (6·12 g.), (β) b. p. 68—70°/700 mm. (1·9 g.), and (γ) b. p. 112—114°/25 mm. (2·2 g.). Gas–liquid chromatography of each fraction was carried out as follows: Fraction (α) contained methyl iodide (4·58 g.) and ethyl iodide (1·52 g.) (2 m. column, C, at 50°). The analysis was repeated with an A column at 60°, the relative retention times being different but the result the same. Fraction (β) was similarly shown to contain methyl iodide (0·3 g.) and ethyl iodide (1·6 g.). Fraction (γ) was analysed by the use of a C column at 196°. There were seven components, three of which had low b. p. The main component (96%) had the same retention

[3] Cadogan, *J.*, 1957, 1079.
[4] Cadogan and Moulden, *J.*, 1961, 5524.

XUM

time as benzyl iodide and diethyl *S*-methyl phosphorothiolate. Slight resolution of these components was obtained by using an A column under the same conditions, but quantitative analysis was impossible.

(ii) *With ethyl iodide.* *S*-Benzyl diethyl phosphorothiolate (1·0 g.) and ethyl iodide (3·0 g., 5·0 mol.) were heated at 105° for 67 hr. No crystals were formed. A portion of the mixture was analysed by gas–liquid chromatography on a C column at 179°; the high-boiling components were thus identified as benzyl iodide (0·3 mole/mole of *S*-benzyl ester) and triethyl phosphorothiolate (12% of benzyl iodide present). The relative retention times were 1 : 1·2). The excess of ethyl iodide was removed by distillation and the residue was extracted with triethylamine, to give benzyltriethylammonium iodide (0·25 g., 0·2 mole/mole of *S*-benzyl ester), m. p. and mixed m. p. 163° (decomp.) on recrystallisation from ethanol–ether. Steinkopf and Bessaritsch [5] reported m. p. 168·5°.

King's College, Strand, London, W.C.2. [*Received, June 29th,* 1961.]

[5] Steinkopf and Bessaritsch, *J. prakt. Chem.*, 1925, **109**, 230.

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## 1084. *Characterisation of Sugars as* p-p′-*Nitrophenylazobenzoyl Derivatives.*

By El S. Amin.

*p-p′*-Nitrophenylazobenzoyl chloride has been used for identification and separation of alcohols,[1] amines,[2] thiols,[3] and amino-acids.[4] It has now been applied to sugars, giving polyacyl derivatives in fairly good yields from eight sugars in pyridine at 0°. The derivatives melt sharply and at much higher temperatures than do other derivatives.[6] They are insoluble in water and of varying solubility in organic solvents. The m. p.s differ sufficiently to be useful criteria, and the sugars can be quantitatively recovered from the esters by hydrolysis.

*Experimental.*—Evaporations were under reduced pressure at 50°.

*Preparations.* The sugar (0·5 mmole) was dissolved in dry pyridine (50 ml.) and cooled to 0°, and *p-p′*-nitrophenylazobenzoyl chloride [1] (4·00 mmoles for monosaccharides and 6·00 mmoles for disaccharides) was added in small portions with cooling. The mixture was kept for 2 weeks at 0°, then filtered through activated alumina (30 g.) that had been wetted with 30 ml. of pyridine. The main (lower) red band was eluted with a 5% solution (90 ml.) of pyridine in benzene; the solvent was removed and the ester purified by crystallisation from acetone. The *derivatives* shown in the Table were thus prepared. The derivatives obtained were predominantly in the α-form.

*p-p′*-Nitrophenylazobenzoates.

| Ester of | M. p. | $[\alpha]_D^{25}$ * | Formula | Found: N (%) | Reqd.: N (%) |
|---|---|---|---|---|---|
| D-Arabinose | 176° | −30° | $C_{57}H_{38}N_{12}O_{17}$ | 14·2 | 14·5 |
| D-Xylose | 174 | +280 | $C_{57}H_{38}N_{12}O_{17}$ | 14·4 | 14·5 |
| α-D-Glucose | 264 | +285 | $C_{71}H_{47}N_{15}O_{21}$ | 14·8 | 14·9 |
| α-D-Fructose | 150 | −130 | $C_{71}H_{47}N_{15}O_{21}$ | 14·9 | 14·9 |
| α-D-Galactose | 254 | +510 | $C_{71}H_{47}N_{15}O_{21}$ | 14·6 | 14·9 |
| α-Lactose | 238 | +350 | $C_{118}H_{78}N_{24}O_{38}$ | 14·0 | 14·2 |
| α-Maltose | 272 | +35 | $C_{118}H_{78}N_{24}O_{38}$ | 13·9 | 14·2 |
| Sucrose | 155 | +40 | $C_{118}H_{78}N_{24}O_{38}$ | 14·4 | 14·2 |

* 5% w/v in $CHCl_3$.

*Recovery.* The ester (260 mg.) was dissolved in dioxan (20 ml.), and methanol (15 ml.) containing sodium methoxide (~12 mg.) was added. The mixture was refluxed for 30 min.,

[1] Hecker, *Chem. Ber.*, 1955, **88**, 1666; Amin and Hecker, *ibid.*, 1956, **89**, 695.
[2] Amin, *J.*, 1957, 3764; 1959, 1619.
[3] Amin, *J.*, 1958, 4769.
[4] Amin, *J.*, 1960, 1953.
[6] Coleman, Farnham, and Miller, *J. Amer. Chem. Soc.*, 1942, **64**, 1501.

then 6N-sodium hydroxide (3 ml.) and water (30 ml.) were added. Refluxing was continued for another 30 min., the solution was diluted to about 200 ml. with water, and 125—150 ml. of solvent were evaporated. The residual solution was filtered, cooled, and made slightly acid with dilute hydrochloric acid. After cooling to allow complete precipitation of *p-p'*-nitrophenylazobenzoic acid, the mixture was filtered to give the sugar quantitatively in the filtrate.

*Chromatography.* A mixture (4 mg.) of pairs of sugar esters in 1 : 4 acetone–chloroform was passed down columns of silica (50 g.) prepared by suspension in 1 : 1 : 1 chloroform–benzene–light petroleum (b. p. 60—80°). The chromatogram was developed with acetone–chloroform and from appropriate zones extraction gave pure esters. Pairs separated were esters of galactose with lactose, of glucose with fructose, maltose, or sucrose, and of lactose with sucrose.

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## 1085. *Interaction of Boron Trichloride with Dioxan and 1,3-Dioxolan.*

By S. COOPER, M. J. FRAZER, and W. GERRARD.

WHEN the 1 : 1 complex [1,2] of dioxan and boron trichloride was heated just above the m. p., exothermic ether fission (1) occurred, the known [3] propensity of 2-chloroethoxyboron

$$C_4H_8O_2,BCl_3 \longrightarrow (Cl{\cdot}CH_2{\cdot}CH_2{\cdot}O)_2BCl + (Cl{\cdot}CH_2{\cdot}CH_2{\cdot}O)_3B + BCl_3 \quad . \quad . \quad . \quad . \quad (1)$$

chlorides to undergo mutual replacement (metathesis) accounting for production of the borate. At 180° under reflux, 1,2-dichloroethane, boric oxide, and boron trichloride were obtained. The 2 : 3 dioxan–boron trichloride complex [2] gave the same compounds. The dioxan–boron tribromide 1 : 1 complex [2] at 30° gave 1,2-dibromoethane and 2-bromoethyl metaborate (2).

$$C_4H_8O_2,BBr_3 \longrightarrow Br{\cdot}CH_2{\cdot}CH_2Br + \tfrac{1}{3}(Br{\cdot}CH_2{\cdot}CH_2{\cdot}O{\cdot}BO)_3 \quad . \quad . \quad . \quad . \quad . \quad (2)$$

In early work,[4] determination of the electric moment of boron trichloride in dioxan indicated co-ordination; but it was stated that the boron chloride caused no decomposition of dioxan, and that boron tribromide reacted violently and formed decomposition products. Later [1] only the 1 : 1 chloro-complex was isolated, and pyrolysis in a vacuum gave unspecified amounts of hydrogen chloride and " 2-vinyloxyethyl dichloroborate," although in another experiment, an unstated amount of a non-volatile tarry residue containing boron and chlorine was obtained.

1,3-Dioxolan did not form an isolable complex with boron trichloride, but immediately underwent ether fission to give chloromethoxyethyl esters (3). The esters have similar spectra, quite different from that of dioxolan. There is absorption in the region 1320—1470 cm.$^{-1}$ which is typical of the ROB structure, there are also bands between 1120 and 1135 cm.$^{-1}$ and at 845 cm.$^{-1}$; further, when $n = 1$ or 2, there is absorption at 940 and 910 cm.$^{-1}$ which we attribute to $-BCl_2$ and $-BCl$, respectively. The products of reactions 5 and 6 give similar spectra, except that the chloro-ethers did not absorb in the region 1320—1470 cm.$^{-1}$. One other feature common to the spectra of all those compounds that contain the chloromethoxy-group is a sharp band at 1724 cm.$^{-1}$ (1613 cm.$^{-1}$ in the case of the dichloroborinate). This could be attributed to coupling between the C–Cl and the C–O–C vibration, but this band is absent from the spectrum of bischloromethyl ether. On

[1] Holliday and Sowler, *J.*, 1952, 11.
[2] Frazer, Gerrard, and Mistry, *Chem. and Ind.*, 1958, 1263.
[3] Edwards, Gerrard, and Lappert, *J.*, 1955, 1470.
[4] Lane, McCusker, and Curran, *J. Amer. Chem. Soc.*, 1942, **64**, 2076.

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being heated the dichloroborinate ($n = 1$) underwent a mutual replacement reaction (4), and the chloroboronate ($n = 2$) afforded 2-chloroethyl chloromethyl ether as one

$$n\overbrace{CH_2{\cdot}O{\cdot}CH_2{\cdot}CH_2{\cdot}O} + BCl_3 \longrightarrow (Cl{\cdot}CH_2{\cdot}O{\cdot}CH_2{\cdot}CH_2{\cdot}O)_nBCl_{3-n} \quad (3)$$

$$2Cl{\cdot}CH_2{\cdot}O{\cdot}CH_2{\cdot}CH_2{\cdot}O{\cdot}BCl_2 \longrightarrow (Cl{\cdot}CH_2{\cdot}O{\cdot}CH_2{\cdot}CH_2{\cdot}O)_2BCl + BCl_3 \quad (4)$$

$$(Cl{\cdot}CH_2{\cdot}O{\cdot}CH_2{\cdot}CH_2{\cdot}O)_2BCl \xrightarrow{heat} Cl{\cdot}CH_2{\cdot}O{\cdot}CH_2{\cdot}CH_2Cl + \text{Other products} \quad (5)$$

$$(Cl{\cdot}CH_2{\cdot}O{\cdot}CH_2{\cdot}CH_2{\cdot}O)_3B \xrightarrow{heat} Cl{\cdot}CH_2{\cdot}O{\cdot}CH_2{\cdot}CH_2{\cdot}O{\cdot}CH_2Cl + (CH_2{\cdot}O)_2B{\cdot}O{\cdot}CH_2{\cdot}CH_2{\cdot}O{\cdot}CH_2Cl \quad (6)$$

decomposition product (5), whereas the borate ($n = 3$) gave 1,2-bischloromethoxyethane and 2-chloromethoxyethyl ethylene borate (6).

*Experimental.*—Where not stated herein, satisfactory analytical data were obtained for all reactants and products. Easily hydrolysed (e.h.) chlorine is that responding to cold water.

*Thermal decomposition of dioxan–boron trihalide complexes.* The tendency of 2-chloroethyl dichloroborinate, and bis-2-chloroethyl chloroboronate to undergo mutual replacement to afford boron trichloride and tris-2-chloroethyl borate hindered the isolation of analytically pure chloroboron compounds. The 1 : 1 boron trichloride complex [1,2] (16·22 g., 3 mol.) was heated to about 95°, whereupon exothermic decomposition occurred, and a temperature of 170° was quickly attained. 0·5 Hr. later the system was at 50°, and distillation at 18 mm. then afforded impure bis-2-chloroethyl chloroboronate (8·77 g.), b. p. 76—83°/18 mm., tris-2-chloroethyl borate (0·37 mol.), b. p. 64°/0·06 mm., $n_D^{20}$ 1·4558, and boron trichloride (0·65 g.) (trap at −80°). The chloroboronate (7·48 g., 1·38 mol.), $n_D^{20}$ 1·4550 (Found: B, 5·5; e.h. Cl, 17·4; Cl, 51·1. Calc. for $C_4H_8BCl_3O_2$: B, 5·3; e.h. Cl, 17·3; Cl, 51·9%), remained after the distilled material had been held at 20°/18 mm. for several hours to attain constancy in e.h. chlorine.

Similarly the 2 : 3 complex,[2] $2C_4H_8O_2,3BCl_3$ (14·03 g., 1 mol.) gave bis-2-chloroethyl chloroboronate (6·5 g., 1·2 mol.) (Found: B, 5·5; e.h. Cl, 17·4; Cl, 51·2%), analysed after being at 20°/0·02 mm. for 12 hr. when the e.h. chlorine content was constant, and tris-2-chloroethyl borate (0·23 mol.), b. p. 68°/0·1 mm., $n_D^{20}$ 1·4558. The trap (−80°) contained boron trichloride (0·93 mol.), and a further trap containing pyridine held boron trichloride (0·32 mol.) as the complex. The 2 : 3 complex lost 6% of its weight at 22°/0·04 mm. in 35 hr.; but the rate of loss was extremely slow by that time. When the 1 : 1 complex (19·0 g.) system was heated at 180° (reflux, 3 hr.) it gave 1,2-dichloroethane (6·62 g.), b. p. 81—82°, $n_D^{20}$ 1·4455. Continued heating gave more of the dichloride (0·95 g.) and a black solid (10·55 g.) (Found: B, 11·2; Cl, 30·0%).

The 1 : 1 tribromide complex [2] (6·02 g., 1 mol.) was heated at 130° for 0·5 hr., to afford 1,2-dibromoethane (0·98 mol.), b. p. 130—131°, $n_D^{20}$ 1·5381, a residue (0·9 g.) (Found: B, 16·1%), and a trap (−80°) condensate (1·07 g.) (Found: B, 1·0; e.h. Br, 6·0%). When the complex (14·45 g.) was heated to 30°, decomposition occurred, and the resultant brown liquid afforded colourless crystals (3·8 g.), m. p. 64—68° (Found: B, 6·9; e.h. Br, 0·0; Br, 53·5. $C_2H_4BBrO_2$ requires B, 7·2; Br, 53·0%) of *2-bromoethyl metaborate.* The infrared spectrum showed absorption bands in the region 1050—1100 cm.$^{-1}$ and also in the region 720—735 cm.$^{-1}$ which are characteristic of metaborates.[5] The filtrate gave 1,2-dibromoethane (8·10 g., 96%), b. p. 129—131°, and a black solid (1·70 g.) (Found: B, 10·6; e.h. Br, 0·0%).

*Interaction of 1,3-dioxolan and boron trichloride.* The dioxolan (1, 2, or 3 mol.) was added dropwise to boron trichloride (14·1 g., 1 mol.) in n-pentane (25 c.c.) at −80°. The 2-chloromethoxyethyl boron ester was held at 20°/20 mm. and then analysed (see Table).

Formation of $(Cl{\cdot}CH_2{\cdot}O{\cdot}CH_2{\cdot}CH_2{\cdot}O)_nBCl_{3-n}$ from 1,3-dioxolan ($n$ mol.).

| | Yield | Found (%) | | Required (%) | | | |
|---|---|---|---|---|---|---|---|
| $n$ | (%) | B | e.h.Cl | B | e.h.Cl | $n_D^{20}$ | $d_{20}^{20}$ |
| 1 | 98·8 | 5·5 | 55·0 | 5·6 | 55·7 | 1·4587 | 1·369 |
| 2 | 97·0 * | 4·0 | 39·9 | 4·1 | 40·2 | 1·4611 | 1·301 |
| 3 | 94·0 | 3·25 | 31·5 | 3·2 | 31·4 | 1·4632 | 1·297 |

* B. p. 46°/0·15 mm.

The dichloroborinate ($n = 1$) (30·96 g.), heated at 45—50°/4·0 mm. for 4 hr., gave the chloroboronate ($n = 2$) (16·1 g., 75%), b. p. 46°/0·15 mm., $n_D^{34}$ 1·4612, and boron trichloride (9·2 g.,

[5] Lappert, *J.*, 1958, 2790.

97·0%). The chloroboronate ($n = 2$) (10·70 g., 96·5%), b. p. 44°/0·15 mm., was also obtained by addition of 1,3-dioxolan (1 mol.) to the dichloroborinate ($n = 1$) (8·00 g., 1 mol.).

Analogously, from the chloroboronate ($n = 2$) (2·75 g., 1 mol.) and 1,3-dioxolan (1 mol.), mixed at −80°, the product then being held at 20°/15 mm. for 7 hr., the borate ($n = 3$) (3·52 g., 100%), $n_D^{20}$ 1·4633, $d_{20}^{20}$ 1·297, was obtained.

The chloroboronate ($n = 2$) (64·37 g.) was held at 50°/20 mm. for 5 hr. Distillation then afforded 2-chloroethyl chloromethyl ether (22·7 g., 73%), b. p. 65°/18 mm., $n_D^{20}$ 1·4568 (Found: e.h. Cl, 27·7; Cl, 55·1. Calc. for $C_3H_6Cl_2O$: e.h. Cl, 27·5; Cl, 55·0%), a liquid (4·52 g.), b. p. 78—82°/18 mm. (Found: B, 0; e.h. Cl, 36·4; Cl, 46·8%), a liquid (3·0 g.), b. p. 102—110°/18 mm. (Found: B, 0; e.h. Cl, 37·4%), a trap (−80°) condensate (4·81 g.), and a non-volatile residue (21·0 g.) (Found: B, 12·5%).

The borate ($n = 3$) (27·6 g.) was heated at 56°/0·3 mm. and distillation afforded a trap (−80°) condensate (2·61 g.), 1,2-bischloromethoxyethane (8·66 g.), b. p. 48—54°/0·3 mm. [redistilled (7·1 g.), b. p. 87°/3·0 mm.] (Found: e.h. Cl, 44·1. Calc. for $C_4H_8Cl_2O_2$: e.h. Cl, 44·6%), and *chloromethoxyethyl ethylene borate* (14·45 g.), b. p. 98—105°/0·3 mm. [redistilled (7·9 g.), b. p. 96—98°/0·3 mm.] (Found: B, 6·1; e.h. Cl, 19·8. $C_5H_{10}BClO_4$ requires B, 6·0; e.h. Cl, 19·7%).

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## 1086. *Thiosuccinimides.*

By R. J. CREMLYN.

SEVERAL succinimides and thioamides are fungitoxic;[1] it was, therefore, decided to prepare a range of thiosuccinimides as potential fungicides. The only known member of this group is *N*-phenylthiosuccinimide which has been prepared by boiling methyl *N*-phenylsuccinamate with phosphorus pentasulphide in toluene,[2] but attempts to repeat this gave very poor yields. However, similar treatment of *N*-phenylsuccinimide with phosphorus pentasulphide afforded a reasonable yield of the monothio-derivative; this method has been extended to the synthesis of *N*-alkyl- and *N*-aryl-thiosuccinimides. In a few cases the dithio-derivatives were also isolated, but their preparation generally required more drastic conditions, under which extensive decomposition occurred, so that in the majority of experiments only the monothiosuccinimides have been obtained. The best procedure for synthesising the monoalkylthiosuccinimides was the interaction of equimolar quantities of succinimide and phosphorus pentasulphide in toluene or xylene at 100° for 1 hour for the lower ($<C_5$) or at the boiling point of the solvent for 3—4 hours for the higher ($>C_5$) homologues.

Reissert and Moré's [2] method for preparing thiosuccinamic acids was not satisfactory, because during neutralisation with hydrochloric acid some loss of sulphur as hydrogen sulphide always occurred, and often was sufficient to prevent isolation of a reasonably pure thiosuccinamic acid.

The thiosuccinimides were characterised by a colour test and by their ultraviolet absorption spectra in absolute alcohol. The *N*-alkyl- and *N*-aryl-thiosuccinimides show two characteristic maxima at 270 and 320 mμ, but the dithio-compounds exhibit only the latter peak, which is known to represent the thiocarbonyl group.[3] The band at 270 mμ is probably a function of the ·CO·$CH_2$·$CH_2$·CS· grouping, because the corresponding *N*-substituted succinimides have no absorption bands in the 200—410 mμ region.[4] When alcoholic solutions of the lower *N*-alkyl ($<C_6$) thiosuccinimides are evaporated at

[1] Searle and Arnold, U.S.P. 2,462,835/1949; Wolf, Closson, and Ligett, U.S.P. 2,726,981/1955; Ludwig and Ross, *Canad. J. Bot.*, 1957, **35**, 65.
[2] Reissert and Moré, *Ber.*, 1906, **39**, 3298.
[3] Braude, *Ann. Reports*, 1945, **42**, 105.
[4] Turner, *J.*, 1957, 4555.

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room temperature, the ultraviolet spectra of the residues showed no absorption peak in this region, indicating that complete exchange of sulphur for oxygen had occurred. A similar reaction has been reported at 60—100° for aqueous solutions of thiosuccinic anhydride.[5] In contrast, *N*-hexylthiosuccinimide showed weak absorption peaks at 270 and 320 mμ after evaporation of the solution, and the higher alkyl- (>$C_6$) and aryl-thiosuccinimides were apparently quite stable.

*Experimental.*—*N*-Alkylsuccinimides were prepared by treating[6] succinic anhydride with the corresponding amine. *N*-Arylsuccinimides were obtained from the intermediate arylsuccinamic acid by dehydration with acetyl chloride.[7]

*Thiosuccinimides.* The *N*-substituted succinimide (1 mole) was dissolved in boiling toluene or xylene, and finely powdered phosphorus pentasulphide (1 mole) gradually added. The mixture was gently boiled under reflux, with stirring, until the solution darkened and the phosphorus pentasulphide disappeared (1—4 hr.), leaving an oily mass adhering to the sides of the flask. The mixture was filtered hot, allowed to cool, and evaporated under reduced pressure. The residue was dissolved in ethanol (charcoal) and filtered. The product was then obtained by standard methods of crystallisation or fractionation under reduced pressure. Details are given in the Tables.

*N*-Alkylthiosuccinimides.

| *N*-Subst. | M. p./b. p. | Yield (%) | Formula | Found (%) C | H | N | S | Required (%) C | H | N | S |
|---|---|---|---|---|---|---|---|---|---|---|---|
| H | 100—104° | 25 | $C_4H_5NOS$ | 41·9 | 4·2 | 11·9 | 27·6 | 41·7 | 4·4 | 12·2 | 27·8 |
| Me | 52—54 | 28 | $C_5H_7NOS$ | 46·2 | 5·3 | 10·7 | 25·3 | 46·5 | 5·4 | 10·8 | 24·9 |
| Bu$^n$ | 95—100/0·2 [a] | 40 | $C_8H_{13}NOS$ | 56·1 | 7·7 | 8·0 | 19·3 | 56·1 | 7·6 | 8·2 | 18·7 |
| Bu$^i$ | 70—75/0·2 | 51 | $C_8H_{13}NOS$ | 56·3 | 7·4 | 8·0 | 19·4 | 56·1 | 7·6 | 8·2 | 18·7 |
| n-$C_5H_{11}$ | 65—70/0·15 [b] | 58 | $C_9H_{15}NOS$ | 57·8 | 7·9 | 7·3 | 17·2 | 58·4 | 8·1 | 7·6 | 17·3 |
| n-$C_6H_{13}$ | 100—105/0·2 [c] | 35 | $C_{10}H_{17}NOS$ | 59·8 | 8·3 | 6·9 | 16·6 | 60·3 | 8·5 | 7·0 | 16·1 |
| Cyclohexyl | 54—56 | 29 | $C_{10}H_{15}NOS$ | 60·4 | 7·6 | 6·5 | 16·9 | 60·1 | 7·6 | 7·1 | 16·2 |
| n-$C_9H_{17}$ | 150—155/0·35 [d] | 65 | $C_{13}H_{21}NOS$ | 63·1 | 10·1 | 6·0 | 13·8 | 63·4 | 10·2 | 5·8 | 13·2 |
| n-$C_{12}H_{25}$ | 145—149/0·2 [e] | 52 | $C_{16}H_{29}NOS$ | 67·3 | 10·1 | 5·1 | 11·0 | 67·8 | 10·2 | 4·9 | 11·3 |

[a] $n_D^{20}$ 1·5589. [b] $n_D^{18}$ 1·5490. [c] $n_D^{20}$ 1·5669. [d] $n_D^{21}$ 1·5420. [e] $n_D^{16}$ 1·5383.

*N*-Arylthiosuccinimides.

| *N*-Subst. | M. p. | Yield (%) | Formula | Found (%) C | H | N | S | Required (%) C | H | N | S |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Ph | 116° [a] | 40 | $C_{10}H_9NOS$ | — | — | — | 17·0 | — | — | — | 16·8 |
| $PhCH_2$ | 60—62 | 44 | $C_{11}H_{11}NOS$ | 63·8 | 5·5 | 6·8 | 16·4 | 64·4 | 5·4 | 6·8 | 15·9 |
| 2-$MeC_6H_4$ | 52—55 | 29 | $C_{11}H_{11}NOS$ | 64·3 | 5·4 | 6·6 | 16·4 | 64·4 | 5·4 | 6·8 | 15·9 |
| 4-$MeC_6H_4$ | 98—100 | 60 | $C_{11}H_{11}NOS$ | 64·5 | 5·6 | 7·0 | 15·3 | 64·4 | 5·4 | 6·8 | 15·9 |
| 2-$ClC_6H_4$ | 92—93 | 57 | $C_{10}H_8ClNOS$ | 53·4 | 3·8 | 6·4 | 13·7 | 53·2 | 3·5 | 6·2 | 14·2 |
| 4-$ClC_6H_4$ | 94—96 | 35 | $C_{10}H_8ClNOS$ | 53·5 | 3·7 | 6·3 | 13·6 | 53·2 | 3·5 | 6·2 | 14·2 |
| 4-$MeOC_6H_4$ | 110—111 | 59 | $C_{11}H_{11}NO_2S$ | 60·2 | 5·1 | 6·1 | 14·2 | 59·8 | 5·4 | 6·3 | 14·5 |
| 2,4-$Me_2C_6H_3$ | 85—88 | 55 | $C_{12}H_{13}NOS$ | 65·5 | 5·8 | 6·3 | 14·7 | 65·8 | 5·9 | 6·4 | 14·6 |
| 2,5-$Me_2C_6H_3$ | 69—72 | 46 | $C_{12}H_{13}NOS$ | 65·6 | 6·0 | 6·7 | 14·5 | 65·8 | 5·9 | 6·4 | 14·6 |
| 2,4-$Cl_2C_6H_3$ | 99—101 | 52 | $C_{10}H_7Cl_2NOS$ | 46·7 | 2·7 | 6·0 | 11·7 | 46·2 | 2·7 | 5·4 | 12·3 |
| 1-$C_{10}H_7$ | 144—145 | 25 | $C_{14}H_{11}NOS$ | 69·6 | 4·6 | 5·8 | 13·9 | 69·7 | 4·6 | 5·8 | 13·3 |

[a] Lit., m. p. 116—117°.

*N*-Alkyldithiosuccinimides.

| *N*-Subst. | M. p./b. p. | Yield (%) | Formula | Found (%) C | H | N | S | Required (%) C | H | N | S |
|---|---|---|---|---|---|---|---|---|---|---|---|
| H | 84—87° | 10 | $C_4H_3NS_2$ | 36·9 | 3·4 | 10·4 | 48·4 | 36·6 | 3·8 | 10·7 | 48·8 |
| Et | 76—79/0·05 | 62 | $C_6H_9NS_2$ | 44·8 | 5·8 | 8·6 | 39·9 | 45·3 | 5·7 | 8·8 | 40·2 |
| Bu$^n$ | 110/0·4 | 15 | $C_8H_{13}NS_2$ | 51·6 | 7·1 | 7·1 | 33·8 | 51·3 | 7·0 | 7·5 | 34·2 |
| n-$C_{10}H_{21}$ | 135—138/0·2 [f] | 32 | $C_{14}H_{25}NS_2$ | 61·3 | 9·5 | 5·8 | 23·4 | 61·8 | 9·2 | 5·2 | 23·6 |
| 1-$C_{10}H_7$ | 168—170 | 20 | $C_{14}H_{11}NS_2$ | 65·5 | 4·5 | 5·5 | 24·4 | 65·4 | 4·3 | 5·4 | 24·9 |

[f] $n_D^{20}$ 1·6112. [g] $n_D^{20}$ 1·5080.

[5] Auger, *Ann. Chim.*, 1891, **22**, 333.
[6] Rice, Reid, and Grogan, *J. Org. Chem.*, 1954, **19**, 884.
[7] Tingle and Cram, *Amer. Chem. J.*, 1907, **37**, 597.

*N-Benzylthiosuccinamic acid.* The following *N*-substituted thiosuccinamic acids were obtained by Reissert and Moré's method:[2] N-*benzyl*, white shining platelets (43%), m. p. 100—102° (from benzene) (Found: C, 59·8; H, 6·4; N, 5·9; S, 14·4. $C_{11}H_{13}NO_2S$ requires C, 59·2; H, 5·8; N, 6·3; S, 14·3%); *N*-phenyl (33%), m. p. 106—108° (lit.,[2] m. p. 106—107°); N-p-*tolyl* (44%), m. p. 122° (Found: C, 60·3; H, 6·0; N, 5·8; S, 13·6. $C_{11}H_{13}NO_2S$ requires C, 59·2; H, 5·8; N, 6·3; S, 14·3%); and N-p-*methoxyphenyl* (70%), m. p. 118—119° (Found: C, 55·9; H, 5·2; N, 6·4; S, 12·6. $C_{11}H_{13}NO_3S$ requires C, 55·2; H, 5·4; N, 5·9; S, 13·4%).

*Colour test.* When a dilute alcoholic solution (2 mg., 5 c.c.) of a thiosuccinimide was treated with one or two drops of a 10% aqueous sodium hydroxide solution, characteristic transient colours developed. The generally observed sequence was the following: Cherry Red ⟶ Dark Blue ⟶ Purple ⟶ Dark Green or Brown.

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## 1087. *Evidence for a Single-stage Two-electron Exchange in the Thallous–Thallic Reaction.*

By A. G. SYKES.

THE kinetics of the reaction $2V^{IV} + Tl^{III} \longrightarrow 2V^{V} + Tl^{I}$ at 80° have been studied with the addition of excess of $Tl^{I}$ and found to be independent of the latter ion.[1] It is concluded that the $Tl^{I}$–$Tl^{III}$ exchange, which is appreciable under the conditions of these experiments, is a single-stage two-electron transfer.

There has recently been much discussion as to whether the simultaneous, or near-simultaneous, transfer of two electrons (possibly by group transfer) is possible for reactions in solution,[2] in particular for oxidation–reduction reactions between metal ions. Of interest in this respect are $Tl^{III} + U^{IV} \longrightarrow Tl^{I} + U^{VI}$ (ref. 3), $Tl^{III} + 2Cr^{II} \longrightarrow Tl^{I} + (Cr^{III})_2$ (ref. 4), and $Tl^{III} + (Hg^{I})_2 \longrightarrow Tl^{I} + 2Hg^{II}$ (ref. 5), which have been discussed earlier,[6] and the $Tl^{I}$–$Tl^{III}$ exchange.[7,8] While single-stage two-electron processes entail greater environmental changes than corresponding one-electron changes do, it may happen that the former are favoured energetically if consecutive one-electron changes require the production of one, or possibly two, unstable intermediates. The kinetics of the $Tl^{I}$–$Tl^{III}$ exchange, with $Tl^{III}$ labelled, give no information concerning the intermediate formation of unstable $Tl^{II}$ ions.

As was reported previously,[6] the kinetics of the $V^{IV}$–$Tl^{III}$ system indicate a mechanism:

$$Tl^{III} + V^{IV} \rightleftharpoons Tl^{II} + V^{V}$$
$$Tl^{II} + V^{IV} \longrightarrow Tl^{I} + V^{V}$$

which is similar to that of the $Fe^{II}$–$Tl^{III}$ reaction.[9] Three experiments were performed at 80°, with initial concentrations of reagents $[V^{IV}] = 0{\cdot}00954$M, $[Tl^{III}] = 0{\cdot}01414$M, $[V^{V}] = 0$, $[H^{+}] = 1{\cdot}8$M, and initial concentrations of $[Tl^{I}] = 0$, $0{\cdot}04431$M, and $0{\cdot}1317$M, respectively. All the reagents used were perchlorates and the ionic strength $I$ was made 3·0M by use of sodium perchlorate. Plots of $[V^{IV}]$ against time were all identical, showing that the

[1] Sykes, Thesis, Manchester University, 1958.
[2] See, *e.g.*, Westheimer, *Chem. Rev.*, 1949, **45**, 419; Higginson and Marshall, *J.*, 1957, 447.
[3] Harkness and Halpern, *J. Amer. Chem. Soc.*, 1959, **81**, 3526.
[4] Ardon and Plane, *J. Amer. Chem. Soc.*, 1959, **81**, 3197.
[5] Armstrong and Halpern, *Canad. J. Chem.*, 1957, **35**, 1020.
[6] Higginson, Rosseinsky, Stead, and Sykes, *Faraday Soc. Discuss.*, 1960, **29**, 49.
[7] Harbottle and Dodson, *J. Amer. Chem. Soc.*, 1951, **73**, 2442.
[8] Prestwood and Wahl, *J. Amer. Chem. Soc.*, 1949, **71**, 3137.
[9] Ashurst and Higginson, *J.*, 1953, 3044.

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initial presence of $Tl^{I}$ in the concentrations stated has a negligible effect; the initial rate of disappearance of $Tl^{III}$ was $0{\cdot}904 \times 10^{-4}$ mole $l.^{-1}$ $min.^{-1}$.

From data by Prestwood and Wahl [8] at 25—50·1°, $[H^+] = 1{\cdot}8$M, and $I = 3{\cdot}68$M, the rate constant for the $Tl^{I}$–$Tl^{III}$ reaction at 80° $\{k = k' + (k''/[H^+])\}$ can be obtained by extrapolating activation-energy plots of $k'$ and $k''$, and is $k = 0{\cdot}272$ $mole^{-1}$ $min.^{-1}$.

More recent work by Gilks and Waind [10] suggests that $k$ will vary for ionic strengths $I = 3{\cdot}0$—$3{\cdot}68$M, but a variation greater than a factor of 2 seems unlikely. The rate of exchange of $Tl^{III}$, $d[Tl^{III}]/dt = -k[Tl^{III}][Tl^{I}]$, is therefore $1{\cdot}70 \times 10^{-4}$ mole $l.^{-1}$ $min.^{-1}$ for the second run and $5{\cdot}06 \times 10^{-4}$ mole $l.^{-1}$ $min.^{-1}$ for the third, *i.e.*, both rates are of the same order as that of the $V^{IV}$–$Tl^{III}$ reaction. Were $Tl^{II}$ an intermediate in the exchange reaction the rate of the $V^{IV}$–$Tl^{III}$ reaction would be expected to increase appreciably on addition of $Tl^{I}$. It is therefore concluded that the $Tl^{I}$–$Tl^{III}$ exchange is by a single two-electron change.

Similar conclusions have recently been reported by Gryder and Dorfman [11] after observations on the $Ce^{IV}$–$Tl^{I}$ system in the presence of $Tl^{III}$.

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[10] Gilks and Waind, *Faraday Soc. Discuss.*, 1960, **29**, 102.
[11] Gryder and Dorfman, *J. Amer. Chem. Soc.*, 1961, **83**, 1254.

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## 1088. *The Thermal Isomerization of Spirobicyclopropane.*

By M. C. FLOWERS and H. M. FREY.

SPIROBICYCLOPROPANE (spiropentane) undergoes a first-order thermal isomerization to give methylenecyclobutane in the temperature range 360—410° C. The isomerization

was carried out in an " aged " Pyrex-glass vessel, and plots that were accurately of first order were obtained for decompositions varying from 20 to 70%. The rate constants for this transformation are:

| | | | | |
|---|---|---|---|---|
| $10^4k$ ($sec.^{-1}$) ..... | 25·4 | 10·4 | 4·13 | 1·53 |
| $t$ (° C) ..... | 408·4 | 394·5 | 380·5 | 366·2 |

The standard deviation of the rate constant at 408·4° is 0·58%.

These data fit the Arrhenius equation $k = 10^{15{\cdot}86} \exp(-57{,}570/RT)$ $sec.^{-1}$ with a standard deviation of less than 10 cal. The very small deviation shows the high reproducibility of the results but is no indication of the true error in the determination of the energy of activation which is probably of the order of ±600 calories resulting largely from temperature uncertainties. The first-order rate constant is independent of pressure from 25 to 350 mm., but fall off has started at 13·5 mm. All the evidence at present strongly suggests this to be a true unimolecular transformation.

In the temperature range where the isomerization occurs the spirobicyclopropane molecule also decomposes to yield one molecule of allene and one of ethylene. This reaction is slower than the isomerization and has a higher energy of activation. At 408° C, some 9% of the reaction proceeds by this path, whereas at 366° C it accounts for about 7% of the products. The reactions of the methylenecyclobutane are scarcely significant under the experimental conditions employed. Its decomposition to allene (and ethylene) accounts for only about 4% of the allene formed. Its isomerization to 1-methylcyclobut-1-ene which appears to be heterogeneous is likewise insignificant.

The observed activation energy of 57,570 cal. is considerably smaller than that for the isomerization of cyclopropane to propene [1] or 1,1-dimethylcyclopropane to 2-methylbut-2-ene and 3-methylbut-1-ene.[2] This is not unexpected since this isomerization, in contrast to those of the cyclopropanes, does not require the breaking of any carbon–hydrogen bonds. The very large pre-exponential factor (even allowing for the degeneracy of 8 in the reaction path) implies a transition state which is very " loose " in comparison with the highly strained spirobicyclopropane structure.

*Experimental.*—Spirobicyclopropane (spiropentane) was prepared from pentaerythritol tetrabromide by the method of Applequist *et al.*[3] Unsaturated impurities were removed by treating the crude product with bromine at −78°. After being washed with sodium carbonate solution and water the spiro-compound was dried and fractionally distilled at −24°. The distillate consisted of spirobicyclopropane (97%) and 1,1-dimethylcyclopropane (3%). This mixture was separated on a preparative gas-chromatographic column (liquid phase, dinonyl phthalate) followed once again by fractionation at −24° and yielded spirobicyclopropane (99·95% pure).

Methylenecyclobutane was prepared from pentaerythritol tetrabromide by the method of Roberts and Sauer.[4] The crude product was fractionally distilled at −24°. The final product contained 2·3% of the spiro-compound and 0·1% of other impurities.

1-Methylcyclobutene was prepared by isomerisation of methylenecyclobutane on a sodium–alumina catalyst.

Allene was prepared from 2,3-dichloropropene and purified by low-temperature fractionation; its purity was 99·8%.

The purity of all compounds was determined by gas chromatography. The absence of impurities of high molecular weight was proved by mass spectrometry.

The Pyrex-glass vessel (1·4 l.) was in a furnace whose temperature could be maintained indefinitely to better than 0·1° c. The temperature gradient over the entire length of the vessel was less than 0·5° c. Diaphragm valves were employed throughout to avoid troubles associated with the absorption of hydrocarbons in stopcock grease. Analysis was by gas chromatography, a 30 ft. × 0·17 in. (i.d.) coiled copper column containing bis-2-cyanoethyl ether on Chromosorb being maintained at 0°. Hydrogen was the flow gas and a Gow-Mac katharometer was the detector. The signals from the katharometer were fed, *via* a variable attenuator, to a 0—1 mv Sunvic recorder fitted with a retransmitting slide-wire. Signals from this slide-wire were used to drive an integrating motor. The analytical precision was better than ±0·5%.

Calibration mixtures were prepared in a specially designed vacuum system which employed only greaseless valves to avoid absorption errors.

We thank the Chemical Society and the Department of Scientific and Industrial Research for grants for equipment. M. C. F. thanks the Esso Petroleum Company for the award of a studentship.

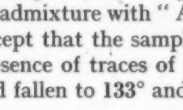
CHEMISTRY DEPARTMENT, SOUTHAMPTON UNIVERSITY. [*Received, May 24th,* 1961.]

[1] Falconer, Hunter, and Trotman-Dickenson, *J.*, 1961, 609.
[2] Flowers and Frey, *J.*, 1959, 3953.
[3] Applequist, Fanta, and Henrikson, *J. Org. Chem.*, 1958, **23**, 1715.
[4] Roberts and Sauer, *J. Amer. Chem. Soc.*, 1949, **71**, 3925.

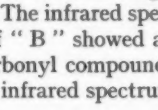
## 1089. *Reactions of Sodium 2-Oxocyclohexyl Thiolsulphate.*

By Brian Milligan and J. M. Swan.

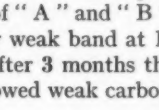
By reaction of 2-chlorocyclohexanone with sodium sulphide, Backer *et al.*[1] prepared a compound, allegedly $C_{12}H_{18}O_2S_2$, m. p. 150°, which they formulated as di-(2-oxocyclohexyl) disulphide (I). We have prepared sodium *S*-2-oxocyclohexyl thiolsulphate (II) by reaction of 2-chlorocyclohexanone with sodium thiosulphate, and have converted it both by the action of sodium sulphide * and by oxidation into a disulphide, m. p. 80°, shown to be the authentic disulphide (I) by elemental analysis, molecular-weight determination, infrared spectral analysis, and by preparation of a bis-2,4-dinitrophenylhydrazone. The preparation of Backer *et al.* was repeated and the substance, m. p. 150°, designated " A," was shown to have the composition $C_{12}H_{20}O_2S_2$ rather than $C_{12}H_{18}O_2S_2$, and by infrared analysis to contain hydroxyl but no carbonyl group. When 2-chlorocyclohexanone was allowed to react with sodium hydrogen sulphide rather than disodium sulphide, another product, " B," was obtained, isomeric with " A," and for which the m. p. varied from 143—144° to 168—170° depending on the solvent used for crystallization and the nature of the glass of the m. p. tube. The melting points of these samples of " B " were depressed on admixture with " A." The infrared spectra of " A " and " B " were virtually identical, except that the samples of " B " showed a very weak band at 1720 cm.$^{-1}$, indicating the presence of traces of a carbonyl compound. After 3 months the melting point of " A " had fallen to 133° and the infrared spectrum showed weak carbonyl absorption.



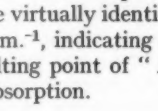
(I)



(II)



(III)



(IV)

α-Mercapto-ketones are known to dimerize readily with formation of 2,5-dihydroxy-1,4-dithians;[2,3,4] we therefore suggest that compounds " A " and " B " are isomers or mixtures of isomers of perhydro-4a,8a-dihydroxythianthren (III), for which six geometrical isomers are possible. Hesse and Jörder[3] have shown that 2,5-dihydroxy-1,4-dithian exists as two geometric isomers, although they were unable to obtain these pure owing to their ready interconversion by way of 2-mercaptoacetaldehyde during crystallization. Hesse and Jörder also believed that the low values obtained for molecular weights (Rast method) were due to partial decomposition to 2-mercaptoacetaldehyde. The low and variable values obtained for the molecular weights of compound (III) (m. p. 150°, *M* 158, 217; m. p. 168—170°, *M* 162) may be explained similarly, as may also the variable melting points of compound " B " and the presence of a weak carbonyl band in the infrared spectra.

Baker and Barkenbus[4] have prepared 1,4-dithiens by reaction of sodium *S*-phenacyl thiolsulphate and several derivatives thereof with ethanolic hydrogen chloride, but the reaction failed with sodium *S*-acetonyl thiolsulphate. However, from a similar reaction with compound (II) we obtained the octahydrothianthren (IV). This compound was also prepared by treatment of perhydro-4a,8a-dihydroxythianthren, m. p. 168—170° with hydrogen chloride, so providing further proof of structure.

* Reactions of thiolsulphates with sodium sulphide often lead to trisulphides, but in this case (as in some others) the corresponding disulphide was obtained (Milligan, Saville, and Swan, *J.*, 1961, 4850.

[1] Backer, Strating, and Huisman, *Rec. Trav. chim.*, 1941, **60**, 381.

[2] Groth, *Arkiv Kemi, Min., Geol.*, 1924, **9**, 63; Hromatka and Engel, *Monatsh.*, 1948, **78**, 29, 38; Haberl, Grass, Hromatka, Brauner, and Preisinger, *ibid.*, 1955, **86**, 551; Haberl and Grass, *ibid.*, p. 599; Geiseler and Stache, *Chem. Ber.*, 1961, **94**, 337.

[3] Hesse and Jörder, *Chem. Ber.*, 1952, **85**, 924.

[4] Baker and Barkenbus, *J. Amer. Chem. Soc.*, 1936, **58**, 262.

*Experimental.*—Light petroleum had b. p. 55—70°. "Woelm" alumina (activity 1) was used for chromatography. M. p.s were determined in soda-glass capillary tubes. Microanalyses and molecular-weight determinations were carried out by the C.S.I.R.O. Microanalytical Laboratory.

*Sodium* S-2-*oxocyclohexyl thiolsulphate* (II). A mixture of 2-chlorocyclohexanone [5] (13·2 g.) and sodium thiosulphate pentahydrate (24·8 g.) in 50% aqueous ethanol (200 ml.) was heated under reflux for 1 hr. and then evaporated to dryness. The residue was extracted with boiling ethanol (100 ml.), and an equal volume of ether added to the extract. The *product* (15·0 g., 65%) separated as flocculent white needles, m. p. 169° (decomp.) (Found: C, 30·8; H, 4·3; S, 27·3. $C_6H_9NaO_4S_2$ requires C, 31·0; H, 3·9; S, 27·6%).

*Di-*(2-*oxocyclohexyl*) *disulphide* (I). (*a*) Bromine water was slowly added with shaking to an aqueous solution of sodium *S*-2-oxocyclohexyl thiolsulphate (II) until a faint yellow colour persisted. This was discharged by addition of a little sodium thiosulphate, and the precipitate was crystallized from aqueous methanol. The *product* separated as colourless needles, m. p. 80° [Found: C, 55·8; H, 7·1; S, 24·6%; *M* (Rast), 242. $C_{12}H_{18}O_2S_2$ requires C, 55·8; H, 7·0; S, 24·8%; *M*, 258], $\nu_{max.}$ 1693s cm.$^{-1}$ (KBr disc). The compound gave a *bis*-2,4-*dinitrophenylhydrazone*, yellow needles, m. p. 221° (from methyl cyanide) (Found: C, 47·1; H, 4·2; N, 18·0; S, 10·2. $C_{24}H_{26}N_8O_8S_2$ requires C, 46·6; H, 4·2; N, 18·1; S, 10·4%).

(*b*) 0·1M-Sodium sulphide (100 ml.) was added dropwise with stirring to a solution of the thiolsulphate (II) (4·6 g.) in phosphate buffer (100 ml.; pH 8) and kept overnight, then filtered. The precipitate was dried and crystallized from light petroleum, giving di-(2-oxocyclohexyl) disulphide (1·1 g.), m. p. 76—79°.

*Perhydro-*4a,8a-*dihydroxythianthren* (III). (*a*) (cf. Backer *et al.*[1]). Hydrogen sulphide was passed into an ice-cold solution of sodium (11·5 g.) in ethanol (250 ml.) until a weight increase of 8·5 g. was recorded. One-fifth of this solution was added dropwise with stirring to a solution of 2-chlorocyclohexanone (13·4 g.) in ethanol (50 ml.) at 0°. After 1 hr. the resulting precipitate was filtered off, dried, and extracted with several portions of boiling benzene. The *product* (0·97 g., 7·5%) crystallized from these extracts; further crystallization from light petroleum or ethanol raised the m. p. to 150° (Found: C, 55·4; H, 7·6; S, 24·6%; *M*, 158, 217. $C_{12}H_{20}O_2S_2$ requires C, 55·3; H, 7·7; S, 24·6%; *M*, 260), $\nu_{max.}$ (OH) 3455 cm.$^{-1}$ (in $CCl_4$), 3322 cm.$^{-1}$ (KBr disc), no absorption in the region 1600—2000 cm.$^{-1}$. After 3 months the m. p. had fallen to 133° and the infrared spectrum showed additional weak absorption at 1720 cm.$^{-1}$ (in $CCl_4$).

(*b*) A solution from sodium (11·5 g.) in ethanol (250 ml.), containing hydrogen sulphide (15·0 g.), was added with stirring to a solution of 2-chlorocyclohexanone (67 g.) in ethanol (250 ml.) at 0°. The precipitate was filtered off, dried, and extracted with boiling benzene, from which separated the product (22·1 g.), m. p. 154—157°. Several crystallizations from butan-1-ol raised the m. p. to 168—170°, but subsequent crystallization from ethanol caused the m. p. to fall to 153°, and, from chloroform, to 143—144°. The m. p. of each sample was depressed on admixture with a sample, m. p. 150°, prepared by method (*a*). A sample, m. p. 168—170°, was dried at 100° for 2 hr. for analysis [Found: C, 55·8; H, 7·8; S, 24·6%; *M*, (Rast), 162. $C_{12}H_{20}O_2S_2$ requires C, 55·3; H, 7·7; S, 24·6%; *M*, 260]. The infrared spectra of $CHCl_3$ solutions of samples, m. p. 168—170°, 153°, and 143—144° were the same as that of the product, m. p. 150°, obtained in (*a*) except for the presence of a very weak carbonyl absorption band at 1720 cm.$^{-1}$. All samples after three successive meltings and resolidifications had m. p.s in the range 125—135°.

1,2,3,4,5,6,7,8-*Octahydrothianthren* (IV). Anhydrous hydrogen chloride was passed through a suspension of sodium *S*-2-oxocyclohexyl thiolsulphate (10 g.) in boiling ethanol (200 ml.). The mixture was evaporated under reduced pressure and the residue partitioned between ethyl acetate and water. The ethyl acetate extract gave an oil (3·0 g.) which was chromatographed in light petroleum on alumina. The *product* (2·3 g.) crystallized from ethanol as prisms, m. p. 97° (Found: C, 63·9; H, 7·3; S, 28·5. $C_{12}H_{16}S_2$ requires C, 64·2; H, 7·2; S, 28·6%), $\nu_{max.}$ (in $CCl_4$) 1611 cm.$^{-1}$ (C:C).

*Dehydration of perhydro-*4a,8a-*dihydroxythianthren.* Anhydrous hydrogen chloride was passed through a boiling solution of perhydro-4a,8a-dihydroxythianthren (2·0 g.; m. p. 168—170°) in dioxan (50 ml.) under reflux for 3 hr. The solution was evaporated and the residue

[5] Newman, Farbman, and Hipsher, *Org. Synth.*, 1945, **25**, 22.

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dissolved in light petroleum and chromatographed on alumina. The first fractions eluted (0·40 g.) were crystallized from ethanol, giving the octahydrothianthren (0·21 g.); m. p. 97°.

The authors thank Drs. W. F. Forbes and E. Spinner for the infrared spectral determinations. Technical assistance by Mr. B. Caldwell is gratefully acknowledged.

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## 1090 *Some Reactions of Sulphur Chloride Pentafluoride.*

By A. G. MASSEY and K. J. PACKER.

SULPHUR CHLORIDE PENTAFLUORIDE is known to break up in the presence of ultraviolet radiation to give $SF_5\cdot$ and $Cl\cdot$ radicals;[1] similarly iron pentacarbonyl loses carbon monoxide to form lower iron carbonyls. It was therefore hoped that reaction of these two compounds would give rise to iron carbonyl derivatives containing sulphur pentafluoride groups. However, the initial experiments showed that sulphur chloride pentafluoride was too vigorous an oxidising agent for iron pentacarbonyl.

There was little reaction at −78°; more than 80% of the sulphur chloride pentafluoride was recovered after 24 hours. When the mixture was warmed to −23° a steady evolution of carbon monoxide commenced but it was impossible to isolate any product since on attempted manipulation, necessarily at room temperature, a vigorous reaction took place in which almost all the carbonyl groups of the iron pentacarbonyl were evolved as carbon monoxide; the remaining volatile material contained carbonyl fluoride, chloride, chloride fluoride, and sulphide. The final residue was a mixture of ferric chloride and fluoride.

Treatment of the iron pentacarbonyl with deficiency of sulphur chloride pentafluoride gave a brown product which contained terminal carbonyl groups but no S–F bonds. If the reaction (with excess of either reagent) was stopped after 5 minutes at room temperature an infrared spectrum of the solid product showed small peaks at 1800 and 1730 $cm.^{-1}$, the region normally associated with bridging carbonyl groups. It is possible that interaction of these bridging carbonyl groups with either sulphur chloride pentafluoride or sulphur tetrafluoride (formed in the initial stages of the reaction) gives rise to the carbonyl halides noted among the products. In support of this is the fact that these peaks disappear when the reaction is allowed to continue; also nickel carbonyl, which does not easily form bridging carbonyl groups, produces no carbonyl halides on reaction with sulphur chloride pentafluoride.

The $Ni(CO)_4$–$SF_5Cl$ reaction is slow at room temperature, about 95% of the carbonyl groups being evolved as carbon monoxide over a period of several hours: $Ni(CO)_4 + SF_5Cl \longrightarrow NiClF_2 + 4CO + SF_4$. Carbon monoxide can be recovered unchanged when mixed with sulphur chloride pentafluoride in Pyrex vessels. However, if the vessel is provided with a quartz side-arm and irradiated with ultraviolet light, interaction takes place, carbonyl fluoride chloride, COFCl, being the predominant product. Small amounts of carbonyl fluoride and carbonyl sulphide are also formed, apparently arising from a side reaction between sulphur tetrafluoride and the carbon monoxide.

*Experimental.*—The volatile materials were handled in a conventional vacuum system; carbon monoxide was measured by means of a Töpler pump. The gaseous reaction products were fractionated and each fraction was weighed before being subjected to infrared analysis; one such fraction often showed infrared peaks corresponding to seven or more compounds.

*Reaction of carbon monoxide with sulphur chloride pentafluoride.* Sulphur chloride pentafluoride (0·82 mmole) and carbon monoxide (4·05 mmoles) were sealed into a vessel provided

[1] Roberts, *Quart. Rev.*, 1961, **15**, 30.

with a quartz side-arm; the quartz was irradiated, at a distance of 5 cm., by a 500-w medium-pressure mercury discharge for 5 hr. 3·66 mmoles of carbon monoxide were removed unchanged; the fraction volatile at −140° (57·6 mg.) contained carbonyl fluoride and chloride fluoride, traces of carbonyl sulphide and sulphur hexa- and tetra-fluoride, and some unchanged sulphur chloride pentafluoride ($COF_2$ : COClF = *ca.* 1 : 15); the fraction volatile at −95° (87·4 mg.) contained carbonyl chloride a little carbonyl chloride fluoride, disulphur decafluoride, sulphur chloride pentafluoride, and small amounts of sulphuryl fluoride and silicon tetrafluoride arising from adventitious hydrolysis of sulphur tetrafluoride and subsequent attack of the glass vessel by the hydrogen fluoride so produced; no products were retained by the −95° trap.

*Reaction of nickel carbonyl with the sulphur chloride pentafluoride.* Nickel carbonyl (0·64 mmole) reacted slowly with sulphur chloride pentafluoride (0·77 mmole) to produce carbon monoxide (2·43 mmoles) in 17 hr. After another 21 hr. a further 0·05 mmole of carbon monoxide was recovered. The fraction volatile at −126° (62·0 mg.) contained mostly sulphur tetrafluoride, but small quantitites of carbonyl sulphide and sulphur chloride pentafluoride were also present; the fraction volatile at −78° (31·2 mg.) contained sulphur chloride pentafluoride and hydrolysis products of sulphur tetrafluoride. Nothing was retained by the −78° trap. The residue, by titration, contained 0·60 mequiv. of chloride ion.

*Reaction of iron pentacarbonyl with sulphur chloride pentafluoride.* Sulphur chloride pentafluoride (0·80 mmole) and iron pentacarbonyl (1·54 mmoles) were allowed to react at −23° for 30 min.; 0·44 mmole of carbon monoxide was removed. The fraction volatile at −78° (16·5 mg.) contained mostly sulphur tetrafluoride together with a little unchanged sulphur chloride pentafluoride. The solid product evolved a further 0·35 mmole of carbon monoxide in another 2 hr. at −23°. After 48 hr. at room temperature, 2·54 mmoles of carbon monoxide and 0·56 mmole of unchanged iron pentacarbonyl were recovered. The residue, on treatment with concentrated nitric acid, produced 0·76 mmole of carbon monoxide; the amount of chloride ion, by titration, was 0·63 mequiv.

*Reaction of an excess of iron carbonyl with sulphur chloride pentafluoride.* Sulphur chloride pentafluoride (0·88 mmole) and iron pentacarbonyl (1·38 mmoles) were allowed to react at room temperature for 96 hr.; 5·32 mmoles of carbon monoxide were evolved. The fraction volatile at −78° (82·0 mg.) contained carbonyl fluoride, sulphide, and chloride fluoride, but no sulphur tetrafluoride or hydrolysis products thereof; nothing was retained by the −78° trap. On treatment with concentrated nitric acid the residues evolved 0·12 mmole of carbon monoxide; the content of chloride ion (by titration) was 0·82 mequiv.

*Reaction of iron carbonyl with an excess of sulphur chloride pentafluoride.* Sulphur chloride pentafluoride (0·85 mmole) and iron pentacarbonyl (0·76 mmole) were allowed to react at room temperature for 144 hr.; 3·49 mmoles of carbon monoxide were evolved. The fraction volatile at −140° (19·5 mg.) contained carbonyl fluoride and sulphide, sulphur tetra- and hexa-fluoride, and a slight remainder of the chloride pentafluoride. The fraction volatile at −95° (118·2 mg.) contained sulphur chloride pentafluoride, sulphuryl fluoride, and silicon tetrafluoride, with traces of carbonyl chloride, fluoride, and sulphide. The fraction involatile at −95° (23·3 mg.) was pure disulphur dichloride (0·17 mmole).

The tube was resealed under a vacuum and heated at 120° for 23 hr.; no carbon monoxide was evolved. The fraction volatile at −140° (17·8 mg.) contained carbonyl sulphide, chloride fluoride, and fluoride, and sulphur tetrafluoride. The remaining fraction (1·6 mg.) was sulphur dioxide. Chloride ion in the residue after hydrolysis amounted to 0·30 mequiv.

*Reaction of carbon monoxide with sulphur tetrafluoride.* Qualitative experiments showed that no carbonyl fluoride was formed when carbon monoxide and sulphur tetrafluoride were left in Pyrex vessels for up to 17 hr. However, when the mixture was irradiated with ultraviolet light through a quartz side-arm, slow reaction was observed in which considerable amounts of carbonyl fluoride and sulphur hexafluoride and traces of carbonyl sulphide were produced.

We are indebted to Imperial Chemical Industries Limited, Alkali Division, for a gift of sulphur chloride pentafluoride, to the Mond Nickel Co. for gifts of nickel and iron carbonyl, and to D.S.I.R. for a maintenance grant (to K. J. P.).

UNIVERSITY CHEMICAL LABORATORY, CAMBRIDGE. [*Received, July 10th,* 1961.]

## 1091. *Studies of the Coal-tar Bases. Part IX.*[1] *A New Method of Isolation of 2,3-Dimethyl- and 2,4,6-Trimethyl-pyridine.*

By R. F. Evans and W. Kynaston.

In this laboratory, the three major components of the commercial β-picoline fraction of coal-tar, 2,6-dimethyl- and 3- and 4-methyl-pyridine, have been separated by fractional distillation in the presence of an azeotrope-forming substance such as acetic or propionic acid.[2] Albert,[3] improving an earlier method,[4] has shown that, if the mixture of bases is first converted into the *N*-oxides, fractional distillation separates the three *N*-oxides from which the parent pyridine bases can be recovered by treatment with phosphorus trichloride.

Accordingly a lutidine fraction containing 2,3-, 2,4-, and 2,5-dimethylpyridine was converted into the *N*-oxides; at −12°, 2,3-dimethylpyridine *N*-oxide separated preferentially. Similarly, the *N*-oxides produced from a mixture of 2,3,6- and 2,4,6-trimethylpyridines deposited 2,3,6-trimethylpyridine *N*-oxide at −12°. Nitration [1] of the mixed *N*-oxides at 100° was accompanied by widespread oxidation and only 26% of the 2,4,6-trimethylpyridine *N*-oxide could be recovered; at 60—80°, oxidation was less and 2,4,6-trimethylpyridine *N*-oxide of 90% purity was recovered. Recycling this *N*-oxide through the nitration procedure did not improve the purity. Hence the *N*-oxide was reduced with iron and acetic acid to the parent 2,4,6-trimethylpyridine which was purified through its hydrochloride.[5]

Lutidine and collidine *N*-oxides can be nitrated if there is a vacant 4-position in the pyridine nucleus. The infrared spectra possess intense bands at 1240~1275 cm.$^{-1}$, characteristic of the *N*-oxide linkage.[6]

*Experimental.*—Microanalyses were carried out by Miss M. Corner and staff of this laboratory. M. p.s are corrected.

*Oxidation of lutidines.* For reference, specimens (5 g.) of 2,3-,[7] 2,4-,[8] and 2,5-dimethylpyridine [8] were separately converted into their *N*-oxides with glacial acetic acid (50 ml.) and 30% hydrogen peroxide (12 ml.) according to Ochiai's procedure.[9] 2,3-Dimethylpyridine *N*-oxide, b. p. 118°/4 mm., and 2,5-dimethylpyridine *N*-oxide, b. p. 86°/0·3 mm., were converted into their 4-nitro-derivatives. 2,4-Dimethylpyridine *N*-oxide, b. p. 91°/0·3 mm., was recovered unchanged from the nitration medium.[10] The oxides are hygroscopic.

2,3-Dimethylpyridine *N*-oxide (1·6 g.) was heated under reflux on the steam-bath for 3½ hr. with concentrated sulphuric acid (3·7 ml.; *d* 1·98) and concentrated nitric acid (1·3 ml.; *d* 1·42). The mixture was poured into ice-water, made alkaline with aqueous sodium hydroxide, and extracted with chloroform. The dried ($Na_2SO_4$) extract, on evaporation, furnished a residue (2·4 g.) which, recrystallised from 96% alcohol, gave *2,3-dimethyl-4-nitropyridine N-oxide*, m. p. 91·5—93° (Found: C, 49·9; H, 5·2; N, 16·4. $C_7H_8N_2O_3$ requires C, 50·0; H, 4·8; N, 16·7%).

2,5-Dimethylpyridine *N*-oxide (1·1 g.) was similarly treated with concentrated sulphuric acid (5 ml.) and concentrated nitric acid (1 ml.) for 1 hr., affording *2,5-dimethyl-4-nitropyridine N-oxide*, m. p. 151—152° (from 96% alcohol) (Found: C, 49·9; H, 4·9; N, 16·5%).

The lutidine mixture investigated was a fraction, b. p. 148—158°, enriched in the 2,3-isomer by removal [8] of 2,4- and 2,5-dimethylpyridine as the hydrochloride and the phenol

[1] Part VIII, Evans, *J.*, 1959, 1312.
[2] Coulson and Jones, *J. Soc. Chem. Ind.*, 1946, **65**, 169.
[3] Albert, *Chem. and Ind.*, 1958, 582.
[4] Ochiai, Ikehara, Kato, and Irekawa, *J. Pharm. Soc. Japan*, 1951, **71**, 1385.
[5] Brown, Johnson, and Podall, *J. Amer. Chem. Soc.*, 1954, **76**, 5556.
[6] Katritzky, *Quart. Rev.*, 1959, **13**, 372.
[7] Wibaut and Kooyman, *Rec. Trav. chim.*, 1944, **63**, 231.
[8] Coulson, Cox, Herington, and Martin, *J.*, 1959, 1934.
[9] Ochiai, *J. Org. Chem.*, 1953, **18**, 534.
[10] Ishikawa, *J. Pharm. Soc. Japan*, 1945, **65**, 6.

complex, respectively. Infrared analysis revealed that the 2,3- and 2,5-isomers together amounted to 40% of this fraction.

This fraction (108 g.) was converted into the *N*-oxides with glacial acetic acid (500 ml.) and 30% hydrogen peroxide (98 ml.) according to Ochiai's procedure.[9] The oxides were distilled and a fraction (102 g.) of b. p. 108—120°/0·3 mm. was cooled to −12° overnight and then filtered. The solid (11·2 g.), on crystallisation from acetone at −12°, afforded 2,3-dimethylpyridine *N*-oxide (5·1 g.), identified by its infrared spectrum.

*Oxidation of collidines.* 2,3,6-Trimethylpyridine [1] (1·9 g.) was oxidised to the *N*-oxide in glacial acetic acid (20 ml.) by 30% hydrogen peroxide (3·7 ml.). *2,3,6-Trimethylpyridine N-oxide*, b. p. 84°/0·2 mm., crystallised from ether–acetone at −12° as a dihydrate, m. p. 63° (Found: C, 56·4; H, 9·3; N, 8·0. $C_8H_{15}NO_3$ requires C, 55·5; H, 8·8; N, 8·1%), $\nu_{max.}$ (in $CHCl_3$) 3380, 1630 cm.$^{-1}$ (OH stretching and OH deformation, respectively), and 1268 cm.$^{-1}$ (N–O).

The *picrate* crystallised from ethanol as yellow needles, m. p. 97—98·5° (Found: C, 45·6; H, 3·8; N, 15·1. $C_{14}H_{14}N_4O_8$ requires C, 45·9; H, 3·9; N, 15·3%).

The collidine fraction, b. p. 106—107°/100 mm., obtained by the refractionation through a 50-plate column of a crude collidine, was shown by infrared analysis to contain 2,3,6-trimethylpyridine (45%) and its 2,4,6-isomer together with a trace of 3-ethylpyridine. This mixture (121 g.) was converted into the *N*-oxides with glacial acetic acid (600 ml.) and 30% hydrogen peroxide (198 ml.) as usual.[9]

The mixed *N*-oxides (76·2 g.; b. p. 98—101°/0·4 mm.) were kept at −12° overnight and the solid (11·7 g.) was collected on a cooled filter. Infrared analysis revealed that the solid was substantially 2,3,6-trimethylpyridine *N*-oxide. The filtrate (62·1 g.), concentrated sulphuric acid (200 ml.; *d* 1·98), and concentrated nitric acid (30 ml.; *d* 1·42) were heated on the steam bath for ¾ hr. at 60° ± 5° and 1 hr. at 75° ± 5°, then poured into ice-cold water (500 ml.), made slightly alkaline with ice-cold concentrated aqueous sodium hydroxide, and filtered. The solid, crystallised from alcohol, furnished 2,3,6-trimethyl-4-nitropyridine *N*-oxide [1] (17·8 g.). Three chloroform extractions of the filtrate, and distillation of the dried ($Na_2SO_4$) chloroform extract, gave 2,4,6-trimethylpyridine *N*-oxide (28 g., 70%), b. p. 80—88°/0·1 mm., of 90—95% purity. Crystallisation of the distillation residue from alcohol at −12° led to the recovery of additional 2,3,6-trimethyl-4-nitropyridine *N*-oxide (1·7 g.; total 67% based on 2,3,6-trimethylpyridine).

A binary mixture (48·2 g.) of collidine *N*-oxides containing 65% of the 2,3,6-isomer afforded 2,3,6-trimethylpyridine *N*-oxide (7·9 g.) on cooling to −15° for 24 hr. The filtrate (33·8 g.), on nitration with concentrated sulphuric acid (104 ml.) and concentrated nitric acid (27 ml.) on the steam bath for 7 hr., afforded a 60% yield of 2,3,6-trimethyl-4-nitropyridine *N*-oxide but only 26% of the 2,4,6-trimethylpyridine *N*-oxide was recovered.

*2,4,6-Trimethylpyridine.* 2,4,6-Trimethylpyridine *N*-oxide (14·9 g.), iron powder (7·5 g.), and glacial acetic acid (150 ml.) were heated on the steam-bath for 2.hr., then made alkaline with aqueous sodium hydroxide and steam distilled. Ether-extraction of the distillate and distillation of the dried ($Na_2SO_4$) extract afforded 2,4,6-trimethylpyridine (9·5 g., 72%), b. p. 170—172°. The infrared spectrum of this material revealed the presence of 5—10% of the 2,3,6-isomer. No improvement could be effected in the purity of the 2,4,6-trimethylpyridine if the *N*-oxide, before reduction, was re-treated with a nitrating mixture. The 2,4,6-trimethylpyridine was finally freed from its 2,3,6-isomer by conversion into the mixed hydrochlorides,[9] followed by one crystallisation from alcohol and decomposition with alkali. Infrared examination confirmed the absence of 2,3,6-trimethylpyridine in the specimen.

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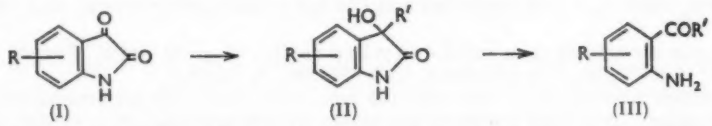
[*Received, July 18th*, 1961.]

XUM

## 1092. *Indoles. Part VI.*[1] *Some Dioxindoles and their Conversion into o-Aminoaryl Ketones.*

By B. Mills and K. Schofield.

Earlier papers in this series described the synthesis of *o*-aminoaryl ketones by the oxidative fission of the 2,3-bond of indole derivatives. The availability of a good range of isatins (I), the possibility of converting these into dioxindoles (II) by reaction with Grignard reagents,[2] and the feasibility of oxidising the dioxindoles to *o*-aminoaryl ketones (III),[3] promised access to compounds not easily obtainable *via* indoles.




Kohn [2] carried out a number of the reactions (I ⟶ II) by adding powdered isatin to an excess of Grignard reagent in ether. More recently [4] a lithium reagent was used instead of the Grignard reagent, and also an attempt was made [5] to overcome some of the disadvantages of Kohn's method by extracting isatin from a Soxhlet thimble into a boiling solution of a Grignard reagent in benzene. Our own experiments, carried out in 1955,[6] were very similar to those of Baumgarten and Creger,[5] but in a number of cases we found it preferable to add the Grignard reagent, in benzene, to a stirred suspension of the isatin in the same solvent rather than to use a Soxhlet apparatus. In the reaction between 4-chloroisatin and phenylmagnesium bromide the immediate product of the reaction was the 1 : 1 complex of 4-chloroisatin and 4-chloro-3-phenyldioxindole. The latter was liberated by passage of the complex, in benzene, over alumina.

Inagaki [3] used alkaline hydrogen peroxide solution to oxidise 3-phenyldioxindole to 2-aminobenzophenone. With some variations in detail this method was successful in all but one of the cases (that of 3-benzyldioxindole) which we examined. However, we found it better to carry out the oxidations by treating solutions of the dioxindoles in alkali with potassium ferricyanide. Whilst hydrogen peroxide gave a cleaner initial product, potassium ferricyanide gave better yields, but it also failed with 3-benzyldioxindole.

The present syntheses of 2-amino-4- and -6-chlorobenzophenone prove the constitution of 4-chloro-2,3-diphenylindole described earlier,[1] for this indole could be converted into 2-amino-6-chlorobenzophenone.

*Experimental.*—*3-Substituted dioxindoles.* The Grignard solution was prepared in ether in the usual way, and the ether was then replaced by benzene. The resulting solution was added dropwise to a suspension of the isatin stirred in benzene, and the mixture was then refluxed, decomposed with dilute sulphuric acid, and steam-distilled. The solid residue was collected and digested with 20% aqueous potassium hydroxide. Filtration and acidification gave the product. The following are notes on the preparations listed in Table 1.

(1) Yellow needles, m. p. 208—209°, from ethanol.

(2) Yellow plates, m. p. 208—210°, from ethanol.

(3) The reaction solution was decomposed with ice and acetic acid. The ether layer was separated, and the aqueous layer was extracted continuously with ether. Evaporation of the combined ether solutions, after being washed and dried, gave the product as yellow needles, m. p. 163—165° (from ethanol).

(4) Yellow needles, m. p. 166—168°, from benzene.

[1] Part V, Ockenden and Schofield, *J.*, 1957, 3175.
[2] Kohn, *Monatsh.*, 1910, **31**, 747; Kohn and Ostersetzer, *ibid.*, 1913, **34**, 789.
[3] Inagaki, *J. Pharm. Soc. Japan*, 1939, **59**, 5.
[4] Bruce, *J.*, 1959, 2366.
[5] Baumgarten and Creger, *J. Amer. Chem. Soc.*, 1960, **82**, 4634.
[6] Mills, Ph.D. Thesis, London, 1955.

(5) The *complex* formed red needles, m. p. 225—228° (Found: C, 59·3; H, 3·3. $C_{14}H_{10}ClNO_2,C_8H_4ClNO_2$ requires C, 59·7; H, 3·2%). Passage of the complex in benzene over alumina gave an almost quantitative yield of *4-chloro-3-phenyldioxindole*, which formed yellow needles, m. p. 259—261° (Found: C, 65·3; H, 3·8. $C_{14}H_{10}ClNO_2$ requires C, 64·7; H, 3·9%), from ethanol.

(6) Yellow needles, m. p. 243—244° (Found: C, 64·0; H, 3·9%), from ethanol.

(7) The reaction mixture was decomposed with ice and dilute hydrochloric acid, and the solid was collected. Fractional crystallisation from ethanol gave golden needles (1·62 g.) of *4-chloro-3-methyldioxindole*, m. p. 240—241° (Found: C, 54·5; H, 3·8. $C_9H_8ClNO_2$ requires C, 54·6; H, 4·0%), and a mixture (0·6 g.) which was not separated further.

TABLE 1.

| Dioxindole | Isatin [a] (g.) | in benzene (c.c.) | Grignard reagent from organic halide (g.) | in benzene (c.c.) | Time of reflux (hr.) | Yield (%) |
|---|---|---|---|---|---|---|
| (1) 3-Phenyl | 1·5 | 50 | 9·6 | 50 | 0·5 | 50 |
| (2) 3-*o*-Tolyl | 5·0 | 250 | 32·0 | 100 | 1 | 60 |
| (3) 3-Methyl [b] | 15·0 | 750 | 72·0 | 300 | 0·25 | 63 |
| (4) 3-Benzyl | 10·0 | 200 | 47·5 | ,, | 3 | 37 |
| (5) 4-Chloro-3-phenyl | 2·0 | 75 | 9·4 | 50 | 24 | 35 [c] |
| (6) 6-Chloro-3-phenyl | 15·0 | 350 | 70·0 | 250 | 3 | 54 |
| (7) 4-Chloro-3-methyl [b] | 5·0 | 200 | 19·5 | 75 | 1 | 30 |

[a] 4- and 6-Chloroisatin were made by the method of Senear *et al.*[7] [b] These experiments were carried out in ether. [c] Of 1 : 1 complex (see below).

*Oxidations with hydrogen peroxide.* The dioxindole in aqueous sodium hydroxide was treated with an excess of hydrogen peroxide. The yellow solution was heated on the steam-bath until oxygen evolution ceased, and the amine was extracted with ether. The details are in Table 2.

TABLE 2.

| Dioxindole | Wt. (g.) | 25% NaOH (c.c.) | $H_2O_2$ (30-vol.) (c.c.) | Yield of amine (%) |
|---|---|---|---|---|
| 3-Phenyl | 0·2 | 3·2 | 2·0 | 52 |
| 3-*o*-Tolyl | 1·0 | 20 | 20 | 76 [a] |
| 3-Methyl | 0·4 | 8 | 12 | 21 [b] |
| 6-Chloro-3-phenyl | 1·5 | 25 | 15 | 45 [c] |
| 4-Chloro-3-methyl | 0·4 | 8 | 12 | 12 [d] |

2-Amino-2′-methylbenzophenone formed yellow needles, m. p. 79—80° (Found: C, 79·4; H, 6·1. Calc. for $C_{14}H_{13}NO$: C, 79·6; H, 6·2%), from aqueous ethanol. [b] The yield of *o*-acetamidoacetophenone (m. p. and mixed m. p. 73—75°) obtained by acetylating the crude reaction product. [c] In small-scale experiments yields up to 95% were obtained. *2-Amino-4-chlorobenzophenone* formed yellow needles, m. p. 83—85° (Found: C, 67·0; H, 3·9. $C_{13}H_{10}ClNO$ requires C, 67·4; H, 4·3%) (from aqueous ethanol). [d] From aqueous ethanol 2-amino-6-chloroacetophenone gave yellow plates, m. p. 88—90° (Found: C, 56·2; H, 4·4. Calc. for $C_8H_8ClNO$: C, 56·6; H, 4·7%).

TABLE 3.

| Dioxindole | Wt. (g.) | KOH in water (g.) | (c.c.) | Ferricyanide in water (g.) | (c.c.) | Crude product (g.) | m. p. |
|---|---|---|---|---|---|---|---|
| 3-*o*-Tolyl | 4·8 | 16·8 | 50 | 13·2 | 30 | 3·8 | 72—76° |
| 3-Methyl | 0·4 | 1·0 | 3·0 | 1·62 | 10 | 0·15 [a] | — |
| 4-Chloro-3-phenyl | 0·1 | 0·35 | 1·1 | 0·25 | 2 | 0·04 [b] | 91—95 |
| 6-Chloro-3-phenyl | 1·5 | 4·9 | 14·7 | 3·6 | 30 | 0·87 | 78—81 |
| 4-Chloro-3-methyl | 0·4 | 1·0 | 3·0 | 1·34 | 10 | 0·05 | 84—87 |

[a] Of *o*-acetamidoacetophenone, formed by acetylating the crude product. [b] 2-Amino-6-chlorobenzophenone separated from aqueous ethanol as yellow prisms, identical with the compound described in the text.

*Oxidations with potassium ferricyanide.* The dioxindole in 30% potassium hydroxide solution was treated with aqueous potassium ferricyanide, and the mixture was heated for 0·5 hr. on the steam-bath. On cooling, the crude amines were collected. For details see Table 3.

[7] Senear, Sargent, Mead, and Koepfli, *J. Amer. Chem. Soc.*, 1946, **68**, 2695.

*Ozonisation of* 4-*chloro*-2,3-*diphenylindole* [by D. W. OCKENDEN]. 4-Chloro-2,3-diphenylindole (0·5 g.) in ethyl acetate (25 c.c.) was ozonised at 0° by the method described earlier.[8] The *ozonide* (0·34 g.) formed prisms, m. p. 172—174° (decomp.) (Found: C, 68·8; H, 4·2. $C_{20}H_{14}ClNO_3$ requires C, 68·3; H, 4·0%). The ozonide (0·25 g.), ethyl acetate (25 c.c.), and 5% palladised charcoal (0·2 g.) were shaken with hydrogen. When the reaction was complete (15 min.) the mixture was filtered and the solvent was removed. 2-*Benzamido*-6-*chlorobenzophenone* formed needles, m. p. 140—141° (Found: C, 72·7; H, 4·4. $C_{20}H_{14}ClNO_2$ requires C, 71·5; H, 4·2%). The amide (0·3 g.), concentrated hydrochloric acid (10 c.c.), and acetic acid (10 c.c.) were boiled for 3 hr. Concentration, basification, and recrystallisation of the product from benzene–ligroin gave 2-*amino*-6-*chlorobenzophenone* (80%), as yellow prisms, m. p. 101—103° (Found: C, 67·7; H, 4·8. $C_{13}H_{10}ClNO$ requires C, 67·4; H, 4·4%), identical with the compound described in Table 2.

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[*Received, July 25th,* 1961.]

[8] Ockenden and Schofield, *J.*, 1953, 612.

## 1093. *Geometrical Isomerism in an Azine.*

By IAN FLEMING and JOHN HARLEY-MASON.

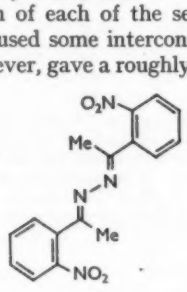
DURING a synthetic study we have made *o*-nitroacetophenone azine from hydrazine and *o*-nitroacetophenone. The azine was a mixture of two separable crystalline forms, yellow prisms, m. p. 135°, and paler yellow needles, m. p. 128°, designated A and B respectively.

The mixture of A and B, after being kept for 4 months in daylight (or after treatment with liquid hydrogen cyanide for one week at room temperature), gave a mixture of A and a third crystalline form, C, very pale yellow prisms, m. p. 166—167°.

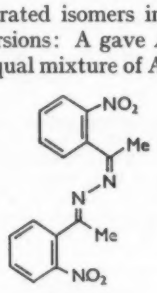
The evidence that A, B, and C are the three theoretically possible geometrical isomers of *o*-nitroacetophenone azine, (I), (II), and (III), is as follows:

(*a*) After separation, forms A, B, and C did not revert to the mixtures on recrystallisation from a variety of solvents.

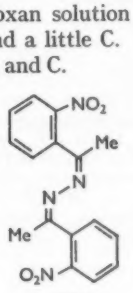
(*b*) Irradiation of each of the separated isomers in dioxan solution with ultraviolet light for 4 hr. caused some interconversions: A gave A and a little C. C gave C and a little A. B, however, gave a roughly equal mixture of A, B, and C.




(I)




(II)




(III)

(*c*) The similar but not identical infrared spectra were consistent with the structure.

(*d*) The ultraviolet spectra, taken in ethanol, were similar but not identical. A and B gave strong end-absorption with no maximum above 210 mμ, the curve of form A being displaced relative to that of B by about 10 mμ to longer wavelengths. The curve of form C was similar in position to that of B, but a maximum at 217 mμ (ε 24,300) was just resolved. All three spectra were similar to that of *o*-nitrobenzaldehyde azine.[1]

(*e*) The nuclear magnetic resonance spectra of forms A and C showed a sharp singlet at τ 7·7 and 7·9, respectively, due to the methyl protons. The spectrum of B, however, showed a symmetrical doublet centred at τ 7·55. This indicates that form B is the unsymmetrical isomer (II), since in this case it is possible for the two methyl groups to be exposed to different shielding effects from the benzene rings.

[1] Ferguson and Branch, *J. Amer. Chem. Soc.*, 1944, **66**, 1467.

The fact that form A is the most abundant and has the strongest ultraviolet and visible absorption indicates that it has the structure (I), which shows the least strain in approaching planarity. Form C, therefore, is assigned structure (III).

To the best of our knowledge this is the first example of the isolation and characterisation of all three possible geometrical isomers of an azine. Dale and Zechmeister [2] were able to separate two forms each of cinnamaldehyde azine and phenylpentadienal azine geometrically isomeric in the azine system. The all-*trans*-forms were crystalline but they obtained the " *cis* I " forms only as oils and no analyses were reported.

*Experimental.*—Nuclear magnetic resonance spectra were obtained for pyridine solutions at 40 Mc./sec. by using a Varian Associates V4300B spectrometer and 12" electromagnet with flux stabilisation and sample spinning. Positions of reference are quoted on the $\tau$ scale [$\tau$ ($SiMe_4$) = 10·00] and have been measured against tetramethylsilane as an internal reference, with the aid of the side-bands generated by a Muirhead-Wigan D695A decade oscillator. The infrared spectra were recorded on a Perkin-Elmer model 21 with a sodium chloride prism, for Nujol and hexachlorobutadiene mulls.

Light petroleum refers to the fraction boiling between 40° and 60°.

o-*Nitroacetophenone azine.* o-Nitroacetophenone (13·2 g.) was refluxed with 100% hydrazine hydrate (2 g.) in ethanol (8 ml.) containing concentrated hydrochloric acid (4 drops) for 7 hr. The mixture was left to cool overnight, to give pale yellow crystals (11·9 g., 92%), m. p. 117—129°.

*Separation of isomers A and B.* The crude azine (1 g.) was dissolved in benzene (20 ml.); to the filtered solution light petroleum (20 ml.) was added, and the mixture kept at room temperature without disturbance for 1 hr. The deep yellow prisms of *form A* were collected (0·2 g.), m. p. 135° (Found: C, 58·7; H, 4·3; N, 17·5. $C_{16}H_{14}N_4O_4$ requires C, 58·9; H, 4·3; N, 17·2%), $\nu_{max.}$ 1621 (C=N), 1576 (Ar), 1536 and 1371 ($NO_2$) cm.$^{-1}$.

The mother liquor was evaporated, the residue dissolved in benzene (7 ml.), to the filtered solution light petroleum (15 ml.) was added, and the mixture kept at room temperature for 24 hr. The precipitated crystals were separated by hand to give *isomer B* as clusters of pale yellow needles (0·1 g.), m. p. 128° (Found: C, 58·5; H, 4·6; N, 17·5%), $\nu_{max.}$ 1626, 1575, 1523, and 1353 cm.$^{-1}$.

*Preparation of isomer C.* o-Nitroacetophenone azine (the mixture of A and B) was kept in a glass bottle in diffused daylight for 4 months. On repeating the separation above, forms A and C crystallised together and were separated by hand. Form C, when recrystallised from acetone, had m. p. 166—167° [Found: C, 58·8; H, 4·7; N, 17·5%; *M* (in $CH_2Cl_2$; cf. Iyengar [3]), 311 ± 20. $C_{16}H_{14}N_4O_4$ requires *M*, 326), $\nu_{max.}$ 1628, 1575, 1523 and 1353 cm.$^{-1}$.

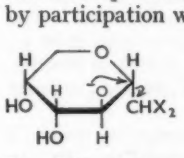
UNIVERSITY CHEMICAL LABORATORY, CAMBRIDGE. [*Received, August 1st*, 1961.

[2] Dale and Zechmeister, *J. Amer. Chem. Soc.*, 1953, **75**, 2384.
[3] Iyengar, *Rec. Trav. chim.*, 1954, **73**, 789.

## 1094. *Diethylsulphonyl-(2-O-methyl-α-D-arabopyranosyl)methane and its Behaviour with Base.*

By L. HOUGH and A. C. RICHARDSON.

THE degradation of diethylsulphonylpyranosylmethane derivatives (*e.g.*, II; R = H) with base proceeds by a nucleophilic mechanism involving the cleavage of the 1,α-bond by participation with a lone pair of electrons on the ring-oxygen atom.[1] In the alkaline hydrolysis of phenyl glycosides the 2-hydroxyl group participates in the elimination of the phenoxide ion.[2] Since an analogous mechanism (cf. A) may be operative in the degradation of the cyclic disulphones, a suitably protected derivative, namely, diethylsulphonyl-(2-*O*-methyl-α-D-arabopyranosyl)methane (II; R = Me), was prepared and its behaviour with base examined.

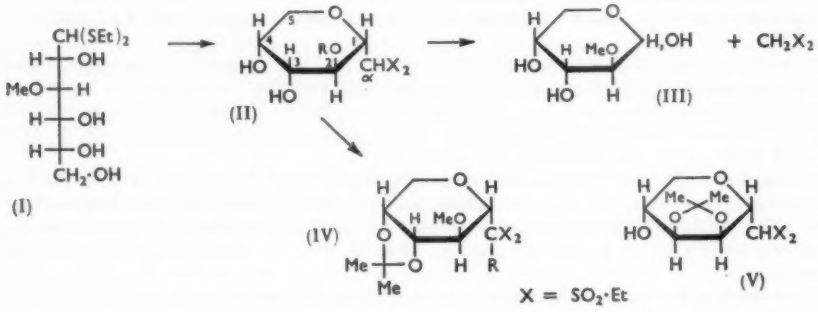


(A)

[1] Hough and Richardson, *Proc. Chem. Soc.*, 1959, 193.
[2] Ballou, *Adv. Carbohydrate Chem.*, 1954, **9**, 59.

3-*O*-Methyl-D-glucose was readily converted into the corresponding diethyl dithioacetal (I) which was oxidised by aqueous peroxypropionic acid to a syrupy disulphone. Periodate oxidation of this sulphone was consistent with the cyclic structure (II; R = Me), since it was rapidly oxidised by one mol. of periodate, after which a slower over-oxidation took place. The molecular rotation ($[M]_D$ +3040° in methanol) was similar to that of α-D-arabopyranosyldiethylsulphonylmethane (II; R = H) ($[M]_D$ +3800°), thus indicating the α-configuration for the diethylsulphonylmethyl group. The structure of the disulphone (II; R = Me) was confirmed by conversion into a syrupy mono-*O*-isopropylidene derivative (IV; R = H) and subsequent *C*-methylation with silver oxide and methyl iodide to the known 1,1-diethylsulphonyl-1-(3,4-*O*-isopropylidene-2-*O*-methyl-α-D-arabopyranosyl)ethane (IV; R = Me).

Diethylsulphonyl-(2-*O*-methyl-α-D-arabopyranosyl)methane (II; R = Me) was readily cleaved by dilute aqueous ammonia into diethylsulphonylmethane and 2-*O*-methyl-D-arabinose (III; R = Me),[3,4] which was characterised by conversion into the crystalline 3,4-*O*-isopropylidene derivative.[4] The degradation was complete after 5 days. Consequently the reaction of diethylsulphonylpyranosylmethane derivatives with base is not analogous to that of the alkali-sensitive glycosides, in as much as the 2-hydroxyl does not




participate in the elimination of the diethylsulphonylmethyl group. It is noteworthy that diethylsulphonyl-(2,3-*O*-isopropylidene-α-D-lyxopyranosyl)methane (V) was stable towards base, but this inhibition has been attributed to steric factors resulting from the superimposition of the five-membered ring on to the six-membered ring.[1]

*Experimental.*—M. p.s were determined on the Kofler micro-heating stage. Evaporations were under reduced pressure. Paper chromatography was carried out by the descending method at room temperature on Whatman No. 1 filter paper with the following mobile phases: (i) butan-1-ol–pyridine–water (10 : 3 : 3 v/v); (ii) butan-1-ol–ethanol–water (40 : 11 : 19 v/v). The compounds were detected with 4% w/v ammoniacal silver nitrate and rates of movement are quoted relative to that of rhamnose ($R_{Rh}$) and the solvent front ($R_F$).

3-O-*Methyl-*D*-glucose diethyl dithioacetal* (I). A mixture of 3-*O*-methyl-D-glucose (2·54 g.), ethanethiol (5 ml.), and concentrated hydrochloric acid (2·5 ml.) was shaken for 2½ hr. The resulting solution was diluted with ethanol and neutralised with lead carbonate. The solution, after filtration, was concentrated to a syrup, which crystallised on addition of ether. The crystals were collected and recrystallised from ether (750 ml.) giving, as three crops (2·66 g., 68%), 3-O-*methyl-*D*-glucose diethyl dithioacetal*, m. p. 72—76°, $[\alpha]_D$ −16·7° (*c* 1·23 in MeOH), $R_{Rh}$ 2·0 (solvent i) and 2·24 (solvent ii) (Found: C, 44·2; H, 8·1; S, 20·6. $C_{11}H_{24}O_5S_2$ requires C, 44·0; H, 8·0; S, 21·3%).

*Oxidation of* 3-O-*methyl-*D*-glucose diethyl dithioacetal with aqueous peroxypropionic acid.* A solution of the dithioacetal (1·18 g.) in 50% aqueous dioxan (20 ml.) was cooled to −10°, an

[3] D. C. C. Smith and Barker, *Chem. and Ind.*, 1952, **30**, 1035.
[4] Huffman, Lewis, F. Smith, and Spriesterbach, *J. Amer. Chem. Soc.*, 1955, **77**, 4346.

excess of aqueous peroxypropionic acid added dropwise with stirring, and the solution then kept at −10° for ½ hr. After a further ½ hr. at room temperature concentration yielded a syrup which was dried under a high vacuum to *diethylsulphonyl*-(2-O-*methyl*-α-D-*arabopyranosyl*)-*methane* (1·35 g.), a glass, $[\alpha]_D$ −8·6° (*c* 6·75 in MeOH), $R_{Rh}$ 1·85 (solvent i) and 2·04 (solvent ii) (Found: C, 37·8; H, 6·5; OMe, 8·8. $C_{11}H_{22}O_9S_2$ requires C, 38·2; H, 6·4; OMe, 9·0%).

Reaction of the 2-*O*-methyl derivative with acetic anhydride containing an equal volume of pyridine or a trace of sulphuric acid yielded a syrupy di-*O*-acetate.

The disulphone (0·054 g.) was treated with 0·01M-sodium metaperiodate (100 ml.) and the uptake of oxidant and the release of formic acid were determined.[5] The following results were obtained:

| Time (hr.) | ½ | 1 | 2½ | 4 | 5½ | 24 | 48 |
|---|---|---|---|---|---|---|---|
| Periodate uptake (mol.) | 0·77 | 0·85 | 1·0 | 1·06 | 1·07 | 1·36 | 1·58 |
| Formic acid (mol.) | 0·08 | 0·13 | 0·13 | 0·11 | 0·26 | 0·45 | 0·72 |

*Treatment of diethylsulphonyl*-(2-O-*methyl*-α-D-*arabopyranosyl*)*methane with dilute aqueous ammonia.* The disulphone (0·23 g.) was dissolved in *ca.* 0·5N-ammonia (10 ml.), and the reaction followed by paper chromatography; one reducing sugar was produced which was indistinguishable from 2-*O*-methylarabinose. Reaction was complete after 5 days, then the reaction mixture was extracted continuously with chloroform to remove diethylsulphonylmethane. The aqueous layer was then concentrated to a pale yellow syrup (0·082 g., 74%) of 2-*O*-methyl-D-arabinose,[3,4] $[\alpha]_D$ −105° (*c* 0·82 in $H_2O$), $R_F$ 0·43 (solvent ii).

A solution of the syrup (0·041 g.) in acetone (10 ml.) containing concentrated sulphuric acid (1 drop) was shaken for 18 hr. with anhydrous copper sulphate (0·5 g.). After neutralisation with ammonia (*d* 0·88; 2 drops) the solution was filtered and the filtrate concentrated to a crystalline residue. Sublimation gave 3,4-*O*-isopropylidene-2-*O*-methyl-D-arabinose [4] (0·016 g.), m. p. 115—117°, $R_{Rh}$ 2·0 (solvent i) (Found: C, 52·5; H, 7·9; OMe, 15·9. Calc. for $C_9H_{16}O_5$: C, 52·9; H, 7·8; OMe, 15·2%).

*Protection and C-methylation of the disulphone.* A mixture of the disulphone (0·64 g.), dry acetone (20 ml.), anhydrous copper sulphate (2 g.), and concentrated sulphuric acid (1 drop) was shaken for 24 hr., neutralised with ammonia (*d* 0·88; 2 drops), filtered, and concentrated to a syrup, which was extracted with ether (2 × 25 ml.). Concentration of the combined extracts afforded the isopropylidene derivative as a colourless syrup (0·48 g.).

This derivative was heated with finely powdered anhydrous calcium sulphate in methyl iodide (15 ml.) for 24 hr. Freshly prepared silver oxide (2 g.) was added in small portions during the first 3 hr. The insoluble material was then removed and the filtrate evaporated to a crystalline residue. Recrystallisation from methanol yielded plates (0·17 g.) of 1,1-diethylsulphonyl-1-(3,4-*O*-isopropylidene-2-*O*-methyl-α-D-arabopyranosyl)ethane, m. p. 175—185° (unchanged on recrystallisation), $[\alpha]_D$ −8·8° (*c* 0·57 in MeOH). The infrared spectrum was identical with that of an authentic sample prepared from α-D-arabopyranosyldiethylsulphonylmethane (II; R = H) by conversion into its 3,4-*O*-isopropylidene derivative and subsequent methylation with silver oxide and methyl iodide.

One of us (A. C. R.) thanks the Department of Scientific and Industrial Research for a Maintenance Award.

THE UNIVERSITY, BRISTOL. [*Received, August 4th*, 1961.]

[5] Hough and Coxon, *J.*, 1961, 1463.

# INTERNATIONAL ATOMIC WEIGHTS, 1961.

The following atomic weights are based on the exact number 12 for the carbon isotope 12, as agreed between the International Unions of Pure and Applied Physics and of Pure and Applied Chemistry.

| Name. | Symbol. | At. No. | At. wt. |
|---|---|---|---|
| Actinium | Ac | 89 | — |
| Aluminium | Al | 13 | 26·9815 |
| Americium | Am | 95 | — |
| Antimony | Sb | 51 | 121·75 |
| Argon | Ar | 18 | 39·948 |
| Arsenic | As | 33 | 74·9216 |
| Astatine | At | 85 | — |
| Barium | Ba | 56 | 137·34 |
| Berkelium | Bk | 97 | — |
| Beryllium | Be | 4 | 9·0122 |
| Bismuth | Bi | 83 | 208·980 |
| Boron | B | 5 | 10·811 ± 0·003 [a] |
| Bromine | Br | 35 | 79·909 [b] |
| Cadmium | Cd | 48 | 112·40 |
| Cæsium | Cs | 55 | 132·905 |
| Calcium | Ca | 20 | 40·08 |
| Californium | Cf | 98 | — |
| Carbon | C | 6 | 12·01115 ± 0·00005 [a] |
| Cerium | Ce | 58 | 140·12 |
| Chlorine | Cl | 17 | 35·453 [b] |
| Chromium | Cr | 24 | 51·996 [b] |
| Cobalt | Co | 27 | 58·9332 |
| Copper | Cu | 29 | 63·54 |
| Curium | Cm | 96 | — |
| Dysprosium | Dy | 66 | 162·50 |
| Einsteinium | Es | 99 | — |
| Erbium | Er | 68 | 167·26 |
| Europium | Eu | 63 | 151·96 |
| Fermium | Fm | 100 | — |
| Fluorine | F | 9 | 18·9984 |
| Francium | Fr | 87 | — |
| Gadolinium | Gd | 64 | 157·25 |
| Gallium | Ga | 31 | 69·72 |
| Germanium | Ge | 32 | 72·59 |
| Gold | Au | 79 | 196·967 |
| Hafnium | Hf | 72 | 178·49 |
| Helium | He | 2 | 4·0026 |
| Holmium | Ho | 67 | 164·930 |
| Hydrogen | H | 1 | 1·00797 ± 0·00001 [a] |
| Indium | In | 49 | 114·82 |
| Iodine | I | 53 | 126·9044 |
| Iridium | Ir | 77 | 192·2 |
| Iron | Fe | 26 | 55·847 [b] |
| Krypton | Kr | 36 | 83·80 |
| Lanthanum | La | 57 | 138·91 |
| Lead | Pb | 82 | 207·19 |
| Lithium | Li | 3 | 6·939 |
| Lutetium | Lu | 71 | 174·97 |
| Magnesium | Mg | 12 | 24·312 |
| Manganese | Mn | 25 | 54·9380 |
| Mendelevium | Md | 101 | — |
| Mercury | Hg | 80 | 200·59 |
| Molybdenum | Mo | 42 | 95·94 |
| Neodymium | Nd | 60 | 144·24 |
| Neon | Ne | 10 | 20·183 |
| Neptunium | Np | 93 | — |
| Nickel | Ni | 28 | 58·71 |
| Niobium | Nb | 41 | 92·906 |
| Nitrogen | N | 7 | 14·0067 |
| Nobelium | No | 102 | — |
| Osmium | Os | 76 | 190·2 |
| Oxygen | O | 8 | 15·9994 ± 0·0001 [a] |
| Palladium | Pd | 46 | 106·4 |
| Phosphorus | P | 15 | 30·9738 |
| Platinum | Pt | 78 | 195·09 |
| Plutonium | Pu | 94 | — |
| Polonium | Po | 84 | — |
| Potassium | K | 19 | 39·102 |
| Praseodymium | Pr | 59 | 140·907 |
| Promethium | Pm | 61 | — |
| Protactinium | Pa | 91 | — |
| Radium | Ra | 88 | — |
| Radon | Rn | 86 | — |
| Rhenium | Re | 75 | 186·2 |
| Rhodium | Rh | 45 | 102·905 |
| Rubidium | Rb | 37 | 85·47 |
| Ruthenium | Ru | 44 | 101·07 |
| Samarium | Sm | 62 | 150·35 |
| Scandium | Sc | 21 | 44·956 |
| Selenium | Se | 34 | 78·96 |
| Silicon | Si | 14 | 28·086 ± 0·001 [a] |
| Silver | Ag | 47 | 107·870 [b] |
| Sodium | Na | 11 | 22·9898 |
| Strontium | Sr | 38 | 87·62 |
| Sulphur | S | 16 | 32·064 ± 0·003 [a] |
| Tantalum | Ta | 73 | 180·948 |
| Technetium | Tc | 43 | — |
| Tellurium | Te | 52 | 127·60 |
| Terbium | Tb | 65 | 158·924 |
| Thallium | Tl | 81 | 204·37 |
| Thorium | Th | 90 | 232·038 |
| Thulium | Tm | 69 | 168·934 |
| Tin | Sn | 50 | 118·69 |
| Titanium | Ti | 22 | 47·90 |
| Tungsten | W | 74 | 183·85 |
| Uranium | U | 92 | 238·03 |
| Vanadium | V | 23 | 50·942 |
| Xenon | Xe | 54 | 131·30 |
| Ytterbium | Yb | 70 | 173·04 |
| Yttrium | Y | 39 | 88·905 |
| Zinc | Zn | 30 | 65·37 |
| Zirconium | Zr | 40 | 91·22 |

[a] Atomic weights so designated are known to be variable because of natural variations in isotopic composition. The observed ranges are:

| | | | |
|---|---|---|---|
| Hydrogen | ±0·00001 | Oxygen | ±0·0001 |
| Boron | ±0·003 | Silicon | ±0·001 |
| Carbon | ±0·00005 | Sulphur | ±0·003 |

[b] Atomic weights so designated are believed to have the following experimental uncertainties:

| | | | |
|---|---|---|---|
| Chlorine | ±0·001 | Bromine | ±0·002 |
| Chromium | ±0·001 | Silver | ±0·003 |
| Iron | ±0·003 | | |

For other elements the last digit is believed to be reliable to ±0·5.

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Alet, I. I
philic
ions in
Ali, S. I.
Allegrini
Allen, C
compl
amine
2171.



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# JOURNAL: INDEX OF AUTHORS, 1961


## A

**Aalbersberg**, W. Ij., **Gaaf**, J., and **Mackor**, E. L., Electron-transfer reactions between oxygen and aromatic hydrocarbons, 905.

**Abel**, E. W. The reactions of hexamethyldisilthiane and ethylthiotrimethylsilane with alcohols, thiols, acids, and amines, 4933.

**Abraham**, R. J., **Jackson**, A. H., and **Kenner**, G. W. The proton magnetic resonance spectra of porphyrins. Part I. The effect of β-substitution on the proton chemical shifts of porphyrins, 3468.

**Acheson**, R. M., **Barltrop**, J. A., **Hichens**, M., and **Hichens**, R. E. The synthesis of some thiophens related to vitamin A, 650.

**Acheson**, R. M., and **Hands**, A. R. Nitroethylene and some indolylmagnesium iodides, 744.

5-Hydroxyskatole, 746.

**Acheson**, R. M., and **Vernon**, J. M. Addition reactions of heterocyclic compounds. Part VIII. Methyl pyrrole-1-carboxylate and dimethyl acetylenedicarboxylate, 457.

**Adams**, D. M., **Chatt**, J., **Guy**, R. G., and **Sheppard**, N. The structure of "cyclopropane platinous chloride," 738.

**Adcock**, B., **Lawson**, A., and **Miles**, D. H. 2-Amino-2-imidazolines and 2-amino-2-oxazolines, 5120.

**Addison**, C. C., and **Coldrey**, J. M. Surface tensions of some molten metal nitrates and nitrites, 468.

**Addison**, C. C., and **Hodge**, N. Reactions of uranium and some uranium compounds with nitrosyl chloride, and with liquid nitrosyl chloride–dinitrogen tetroxide mixtures, 2490.

The reaction of uranium with solutions of alkylammonium nitrates in dinitrogen tetroxide; some properties of alkylammonium uranyl nitrates, 2987.

**Addison**, C. C., **Kilner**, M., and **Wojcicki**, A. Nitratopentacarbonylmanganese(I), 4839.

**Addison**, W. E., and **Walton**, A. Intracrystalline oxidation of hydrogen sulphide, 4741.

**Addy**, J. K., **Laird**, R. M., and **Parker**, R. E. The mechanism of epoxide reactions. Part III. The reactions of *p*-bromo-(1,2-epoxyethyl)benzene and *p*-(1,2-epoxyethyl)toluene with benzylamine, 1708.

**Ahmad**, M. S., and **Baddeley**, G. Intramolecular acylation. An attempt to cyclise β-(8-oxo-2-tetralyl)propionic and γ-(8-oxo-2-tetralyl)butyric acids, 2520.

The interaction of decalin and isobutyryl chloride–aluminium chloride, 4303.

**Ahmad**, Y., and **Hey**, D. H. 8-Phenylisoquinolines, 3882.

**Akisanya**, A., **Bevan**, C. W. L., **Halsall**, T. G., **Powell**, J. W., and **Taylor**, D. A. H. West African timbers. Part IV. Some reactions of gedunin, 3705.

**Albert**, A., **Armarego**, W. L. F., and **Spinner**, E. Quinazolines. Part I. Cations of quinazoline. Part III. The structure of the hydrated quinazoline cation, 2689, 5267.

**Albert**, A., and **Matsuura**, S. Pteridine studies. Part XV. The reduction of 2-hydroxypteridine, 5131.

**Albert**, A., and **Reich**, F. Pteridine studies. Part XIII. Addition to 6-hydroxypteridines, 127.

**Alet**, I. R., and **England**, B. D. A comparison of the nucleophilic reactivity of ethoxide, methoxide, and hydroxide ions in dioxan, 5259.

**Ali**, S. I. See **Maxted**, E. B., 4137.

**Allegrini**, E. See **Bun-Hoi**, N. P., 4836.

**Allen**, C. R., **Brook**, A. J., and **Caldin**, E. F. The kinetics of complex-formation of 1,3,5-trinitrobenzene with diethylamine and other amines in solution at low temperatures, 2171.

**Allen**, J. F., and **Chapman**, N. B. Di-*N*-substituted 2-halogenoethylamines. Part IV. *NN*-Bis-2′-aryloxyethyl derivatives: syntheses, reactivity, and pharmacology, 1076.

**Allen**, M. J. Suppression of 1,3-diaxial interaction in methyl reserpate during alkaline hydrolysis, 4252.

**Allen**, M. J., **Cohen**, M., **Pierson**, W. G., and **Siragusa**, J. A. Further studies on the preparation of symmetrical pinacols by cathodic reduction, 757.

**Allen**, M. J., **Pierson**, W. G., and **Siragusa**, J. A. The preparation of mixed pinacols by cathodic reduction. Part II, 2081.

**Allen**, M. J., and **Vikin**, J. Polarographic behaviour of 2-methyl-1,2-di-3′-pyridylpropan-1-one, 1420.

**Allison**, J. M., **Lawrie**, W., **McLean**, J., and **Beaton**, J. M. Dehydrogenation with mercuric acetate in the lupane series. Part II. Lupeol and its derivatives, 5224.

**Allison**, J. M., **Lawrie**, W., **McLean**, J., and **Taylor**, G. R. Dehydrogenation with mercuric acetate in the lupane series. Part I. Betulin and betulinic acid, 3353.

**Allport**, D. C. See **Bu'Lock**, J. D., 1654.

**Alner**, D. J., and **Lansbury**, R. C. The stability constants of the silver complexes of some *NN*-substituted 2-hydroxyethylamines, 3169.

**Altman**, Y., and **Ginsburg**, D. Alicyclic studies. Part XV. Preparation and reactions of 3,3′-bi-indenyl and 2,3:2′,3′-dibenzobi(cycloheptа-2,7-dienyl), 1498.

**Ames**, D. E., and **Islip**, P. J. A new synthesis of long-chain acetylenic acids and some attempts to prepare pure *cis*-olefinic acids, 351.

Syntheses of long-chain acids. Part II. A synthesis of linoleic acid, 4409.

**Amin**, E. S. Characterisation of sugars as *p*-*p*′-nitrophenylazobenzoyl derivatives, 5544.

**Anderson**, D. M. W., **Bell**, F., and **Duncan**, J. L. Some condensation products of malononitrile, 4705.

**Anderson**, D. M. W., **Bews**, A. M., **Garbutt**, S., and **King**, N. J. Studies on uronic acid materials. Part IV. Aqueous decarboxylation of uronic acids, and the decarboxylation of pectic materials during extraction, 5230.

**Anderson**, D. M. W., and **Duncan**, J. L. The molecular structure of some products from the Ehrlich–Sachs reaction, 1631.

**Anderson**, D. M. W., **Duncan**, J. L., and **Rossotti**, F. J. C. The hydrogen bonding of pyrazole in carbon tetrachloride solution, 140.

The hydrogen bonding of imidazole in carbon tetrachloride solution, 2165.

The hydrogen bonding of some substituted pyrazoles in carbon tetrachloride solution, 4201.

**Anderson**, D. M. W., and **King**, N. J. Polysaccharides of the Characeae. Part I. Preliminary examination of a starch-type polysaccharide from *Nitella translucens*. Part IV. A non-esterified pectic acid from *Nitella translucens*, 2914, 5333.

**Anderson**, D. W. See **Ellis**, A. J., 1765, 4678.

**Andrews**, E. D., and **Harvey**, W. E. Some compounds derived from *o*-2-carboxyethylbenzoic acid, 4687.

**Andrews**, K. J. M. Synthesis of quinol monophosphates from vitamin $K_1$, ubiquinone, and other quinones and experiments on oxidative phosphorylation, 1808.

**Angell**, C. L. An infrared spectroscopic investigation of nucleic acid constituents, 504.

**Angyal**, S. J., and **Bender**, V. Cyclitols. Part XI. The constitution of liriodendritol, 4718.

**Angyal**, S. J., and **Tate**, M. E. Cyclitols. Part X. Myoinositol phosphates, 4122.




XUM

**Angyal**, S. J., **Tate**, M. E., and **Gero**, S. D. Cyclitols. Part IX. Cyclohexylidene derivatives of myoinositol, 4116.

**Ansell**, M. F., and **Brooks**, G. T. Reduced cyclic compounds. Part X. The synthesis of 1-1′-acetoxyvinyl-3,4-dihydronaphthalene and its reactions with some dienophils, 201.

**Ansell**, M. F., **Brooks**, G. T., and **Knights**, B. A. The synthesis of four dimethylchrysenes, 212.

**Ansell**, M. F., and **Culling**, G. C. Reduced cyclic compounds. Part XIII. The reaction of 1-1′-acetoxyvinylcyclohexene with *p*-benzoquinones containing a methoxycarbonyl group, 2908.

**Ansell**, M. F., and **Ducker**, J. W. Reduced cyclic compounds. Part XI. The cyclisation of ω-arylalkenoic acids, 206.

**Ansell**, M. F., and **Knights**, B. A. Reduced cyclic compounds. Part XII. Further Diels–Alder reactions of 1-1′-acetoxyvinylcyclohexene, 2903.

**Ansell**, M. F., and **Thomas**, D. A. The preparation of the geraniolenes, 539.

**Apsimon**, J. W., **Green**, B., and **Whalley**, W. B. Sandaraco- and crypto-pimaric acid, 752.

**Archibald**, A. R., **Fleming**, I. D., **Liddle**, A. M., **Manners**, D. J., **Mercer**, G. A., and **Wright**, A. α-1,4-Glucosans. Part XI. The absorption spectra of glycogen– and amylopectin–iodine complexes, 1183.

**Arcus**, C. L., and **Barrett**, G. C. Reactions of organic azides. Part X. The Schmidt reaction with 3′-oxoindeno(2′,1′-2,3)-thiophen: the structure of the product, 1408.

**Arcus**, C. L., and **Halliwell**, A. Poly-(*m*-aminostyrene) and the copolymer with styrene. Kinetics of the decomposition of poly-(*m*-styrenediazonium chloride) and related diazonium chlorides, 3708.

**Arcus**, C. L., and **Howard**, T. J. Olefinic additions with asymmetric reactants. Part VI. Dissymmetric hydrogenation of (±)-4-phenylpent-3-en-2-ol, 670.

**Ariyan**, Z. S., and **Suschitzky**, H. Heterocyclic compounds of chalcone type, 2242.

**Ariyan**, Z. S., and **Wiles**, L. A. The action of sulphur monochloride on aromatic hydrocarbons, 4510.

**Armarego**, W. L. F. Quinazolines. Part II. 1,4- and 3,4-Dihydroquinazoline, 2697.

**Armarego**, W. L. F. See also **Albert**, A., 2689, 5267.

**Armitage**, R., **Bayliss**, G. S., **Gramshaw**, J. W., **Haslam**, E., **Haworth**, R. D., **Jones**, K., **Rogers**, H. J., and **Searle**, T. Gallotannins. Part III. The constitution of Chinese, Turkish, sumach, and tara tannins, 1842.

**Armitage**, R. See also **Haslam**, E., 1836.

**Armour**, C., **Bunton**, C. A., **Patai**, S., **Selman**, L. H., and **Vernon**, C. A. Mechanisms of reactions in the sugar series. Part III. The acid-catalysed hydrolysis of t-butyl β-D-glucopyranoside and other glycosides, 412.

**Arnott**, S., **Davie**, A. W., **Robertson**, J. M., **Sim**, G. A., and **Watson**, D. G. The structure of limonin: *X*-ray analysis of epilimonol iodacetate, 4183.

**Aroney**, M., **Chia**, L. H. L., and **Le Fèvre**, R. J. W. Molecular polarisability: the dipole moment, molar Kerr constant, and space formula of Tröger's base as a solute in benzene, 4144.

**Aroney**, M., **Izsak**, D., and **Le Fèvre**, R. J. W. Molecular polarisability: the dipole moments, polarisations, and molar Kerr constants of ten aliphatic ketones as solutes in carbon tetrachloride, 4148.

**Aroney**, M., **Le Fèvre**, R. J. W., and **Lenthen**, P. M. Molecular polarisability: molar Kerr constants, apparent dipole moments, and conformations of trialkyl borates as solutes, 4140.

**Arotsky**, J., **Mishra**, H. C., and **Symons**, M. C. R. Unstable intermediates. Part XIII. Iodine cations in solution, 12.

**Arthur**, H. R., and **Hui**, W. H. A new triterpene from the Hong Kong Ericaceae: an epoxyglutinane from *Rhododendron westlandii*, 551.

**Arthur**, H. R., and **Loh**, L. Y. S. An examination of the Rutaceae of Hong Kong. Part VIII. The synthesis of the alkaloid, graveoline, 4360.

**Arthur**, H. R., **Tam**, S. W., and **Ng**, Y. L. An examination of the Rutaceae of Hong Kong. Part VII. The essential oils, 3551.

**Ashmore**, P. G., and **Tyler**, B. J. The formation and thermodynamic properties of nitrous acid vapour, 1017.

**Asperger**, S., **Pavlović**, D., and **Orhanović**, M. Mechanism of replacement of chlorine in *cis*- and *trans*-chloronitrobis-(ethylenediamine)cobalt(III) ions by thiocyanate in methanol, 2142.

**Aspinall**, G. O., and **Christensen**, T. B. *Anogeissus schimperi* gum, 3461.

**Aspinall**, G. O., and **Fanshawe**, R. S. Pectic substances from lucerne (*Medicago sativa*). Part I. Pectic acid, 4215.

**Aspinall**, G. O., **Greenwood**, C. T., and **Sturgeon**, R. J. The degradation of xylans by alkali, 3667.

**Aspinall**, G. O., and **Ross**, K. M. The synthesis of 4-*O*-β-D-xylopyranosyl-D-xylose and 3-*O*-methyl-4-*O*-(β-D-xylopyranosyl)-D-xylose, 3674.

**Asscher**, M., and **Vofsi**, D. Chlorine activation by redox-transfer. Part I. The reaction between aliphatic amines and carbon tetrachloride, 2261.

**Atkins**, V. M., and **Monk**, C. B. The dissociation constants of some chlorides and perchlorates in aqueous acetone from conductance measurements, 1817.

**Attenburrow**, J., **Connett**, J. E., **Graham**, W., **Oughton**, J. F., **Ritchie**, A. C., and **Wilkinson**, P. A. Compounds related to the steroid hormones. Part V. The partial synthesis of 21-acetoxy-17-hydroxy-16β-methyl-5α-pregn-9-ene-3,20-dione, 4547.

**Aubrey**, D. W., **Lappert**, M. F., and **Pyszora**, H. Cyclic organic boron compounds. Part V. Infrared spectra of borazoles and boroxoles, 1931.

**Austin**, A. T., and **Howard**, J. The steric course of lactonisation following the deamination of glutamic acid, glutamine, and γ-aminovaleric acid, 3278.

The deamination by nitrous acid, of amino-acids, structurally related to glutamic acid: γ-aminobutyric, γ-aminovaleric, α-aminoadipic, and δ-aminovaleric acid, and isoglutamine, 3284.

The reaction of nitrous acid with glutamine and glutamic acid, 3593.

**Autrey**, R. L., **Barton**, D. H. R., **Ganguly**, A. K., and **Reusch**, W. H. Photochemical transformations. Part XI. The photochemistry of pentacyclic triterpenoids with diene unsaturation in ring C, 3313.

**Axelrod**, L. R. See **Rao**, P. N., 4769.

**Ayres**, D. C., and **Denney**, R. C. Lignans. Part I. Acylation in polyphosphoric acid as a route to intermediates, 4506.

**Aziz**, G. See **Tadros**, W., 2684.

## B

**Bacon**, N., **Brewis**, S., **Usher**, G. E., and **Waight**, E. S. Reaction products from mesityl oxide and lithium, 2255.

**Bacon**, R. G. R., and **Guy**, R. G. Thiocyanogen chloride. Part IV. Reaction with aromatic hydrocarbons; heterolytic and homolytic substitution in benzene homologues, 2428.

**Bacon**, R. G. R., **Guy**, R. G., and **Irwin**, R. S. Thiocyanogen chloride. Part V. Heterolytic and homolytic thiocyanation of alkylnaphthalenes, 2436.

**Bacon**, R. G. R., and **Irwin**, R. S. Thiocyanogen, thiocyanates, and isothiocyanates. Part I. Homolytic substitution in arylalkyl hydrocarbons by thiocyanogen, 2447.

**Baddar**, F. G., **El-Newaihy**, M. F., and **El-Zimaity**, M. T. β-Aroylpropionic acids. Part XX. Conversion of β-(2,5-dimethylbenzoyl)-α- and -β-phenylpropionic acid into polynuclear compounds, 2701.

**Baddar**, F. G., **Ghaly**, E. H., and **El-Newaihy**, M. F. Phenylpropiolic acids. Part VII. The self-condensation of 2-methoxy-4- and -5-methylphenylpropiolic acid, 2528.

**Baddar**, F. G., and **Sherif**, S. β-Aroylpropionic acids. Part XVIII. Their conversion into 4,5-diarylfuran-2,3-dicarboxylic acids, 707.

**Baddar**, F. G. See also **El-Abbady**, A. M., 1083.

**Baddeley**, G., and **Heaton**, B. G. The interaction of decalin, propionyl chloride, and aluminium chloride, 4306.

**Baddeley**, G., **Heaton**, B. G., and **Rasburn**, J. W. The interaction of decalin and Friedel–Crafts acetylating agents. Part III. Part IV, 3828, 3835.

**Baddeley**, G., and **Rasburn**, J. W. The preparation of novel decalin derivatives from 10β-(1,2-dihydroxyethyl)-*trans*-1β-decalol, 3838.

**Baddeley,** G., and **Smith,** N. H. P. Interdependence of molecular conformation and conjugation in aromatic ethers. Part IV, 2516.

**Baddeley,** G. See also **Ahmad,** M. S., 2520, 4303.

**Baddeley,** G. V., **Halsall,** T. G., and **Jones,** E. R. H. The chemistry of triterpenes and related compounds. Part XL. Final clarification of the stereochemistry of hydroxyhopanone, 3891.

**Baddiel,** C. B. See **Cullis,** C. F., 5449.

**Baddiley,** J., **Buchanan,** J. G., and **Hardy,** F. E. Synthesis of 4-*O*-(β-D-glucopyranosyl)-D-ribitol, a degradation product of the ribitol teichoic acid from the walls of *Bacillus subtilis*, 2180.

**Baddiley,** J., **Hughes,** N. A., and **James,** A. L. Synthesis of guanosine diphosphate glucose, 2574.

**Badger,** G. M., and **Kimber,** R. W. L. The formation of aromatic hydrocarbons at high temperatures. Part XIV. The pyrolysis of [α-$^{14}$C]ethylbenzene, 3407.

**Badger,** G. M., and **Novotny,** J. The formation of aromatic hydrocarbons at high temperatures. Part XII. The pyrolysis of benzene. Part XIII. The pyrolysis of 3-vinylcyclohexene, 3400, 3403.

**Badger,** G. M., and **Sasse,** J. M. So-called "2-triacetylthiophen" (a boron compound), 746.

**Bagnall,** K. W., **Deane,** A. M., **Markin,** T. L., **Robinson,** P. S., and **Stewart,** M. A. A. Some acetamide complexes of the actinide tetrachlorides. Part I. Uranium, neptunium, and plutonium, 1611.

**Bagnall,** K. W., **Robinson,** P. S., and **Stewart,** M. A. A. The uranium(IV) nitrates, 4060.

**Bailey,** A. J., **Barker,** S. A., **Moore,** R. H., and **Stacey,** M. Effects of γ-radiation. Part V. Irradiation of cyclohexene and cyclohexanol, 4086.

**Bailey,** E. J., **Elks,** J., **Oughton,** J. F., and **Stephenson,** L. Compounds related to the steroid hormones. Part IV. Dienone–phenol rearrangement of steroid $\Delta^{1,4}$-3,11-diketones, 4535.

**Baillie,** M. J., and **Brown,** D. H. Tungstate and molybdate complexes with tartaric, malic, and succinic acid, 3691.

**Bain,** B. M., and **Saxton,** J. E. The reaction of nicotinic acid 1-oxide and 3-picoline 1-oxide with acetic anhydride, 5216.

**Bairsted,** D. J., and **Whitehurst,** J. S. The tautomerism of $\Delta^{1(9)}$-octal-2-one, 4089.

**Baker,** F. C. See **Mann,** F. G., 3845.

**Baker,** J. A., and **McCrea,** P. A. Substituted linoleic acids, 3854.

**Baker,** R., and **Eaborn,** C. Aromatic reactivity. Part XX. Diphenyl ether, diphenyl sulphide, dibenzofuran, and dibenzothiophen in detritiation, 5077.

**Baker,** R., **Eaborn,** C., and **Taylor,** R. Aromatic reactivity. Part XIX. Detritiation of [*o*- and *p*-$^3$H$_1$]-toluene and -t-butylbenzene, 4927.

**Baker,** W., **Barton,** J. W., **McOmie,** J. F. W., **Penneck,** R. J., and **Watts,** M. L. Biphenylenes. Part V. Some di- and tetra-methoxybiphenylenes, 3986.

**Baker,** W., and **Burrows,** B. F. Tetramethylethylene sulphate, 2257.

**Baker,** W., **Hilpern,** J. W., and **McOmie,** J. F. W. The action of *N*-bromosuccinimide on 1,2,3,4-tetraphenylcyclobutane, 479.

**Baker,** W., **McOmie,** J. F. W., **Pope,** G. A., and **Preston,** D. R. Benzocyclobutenes. Part I. Attempted syntheses of 1,2-diphenylbenzocyclobutene, 2965.

**Baker,** W., **McOmie,** J. F. W., and **Preston,** D. R. Benzocyclobutenes. Part II. A new synthesis of benzocyclobutene and of 1,2-diphenylbenzocyclobutene, 2971.

**Bakshi,** S. P., and **Turner,** E. E. Reduction of cholesteryl benzoylformate (phenylglyoxylate), 168.

The hydratropic acids and the related 2-phenylpropanols, 171.

**Balaban,** A. T., and **Nenitzescu,** C. D. Pyrylium salts obtained by diacylation of olefins. Part II. The two pyrylium salts formed in diacetylation of 2-methylbut-2-ene. Part III. Diacylation of cyclic olefins and a novel synthesis of isoquinoline derivatives, 3553, 3561.

Reaction of pyrylium salts with alkali cyanides, 3566.

**Balaban,** A. T., **Nenitzescu,** C. D., **Gavat,** M., and **Mateescu,** G. Pyrylium salts obtained by diacylation of olefins. Part IV. Di- and tri-acetylation of allybenzene, 3564.

**Baldwin,** M. E. The infrared spectra of cobalt(III) ethylenediamine complexes. Part II. Compounds containing the thiocyanate group, 471.

Sulphitobis(ethylenediamine)cobalt(III) complexes, 3123.

**Baldwin,** M. E., **Chan,** S. C., and **Tobe,** M. L. The mechanism and steric course of octahedral aquation. Part IV. The aquation of *cis*- and *trans*-dichloro- and *cis*- and *trans*-chlorohydroxo-bis(ethylenediamine)cobalt(III) salts, 4637.

**Bamford,** C. H., and **Block,** H. The initiation step in the polymerization of *N*-carboxy-α-amino-acid anhydrides. Part I. Catalysis by tertiary bases. Part II. Effects related to the structure of amine initiators, 4989, 4992.

**Bamford,** C. H., **Block,** H., and **Pugh,** A. C. P. The polymerization of 3-substituted oxazolidine-2,5-diones, 2057.

**Bancroft,** G., **Haddad,** Y. M. Y., and **Summers,** G. H. R. Some reactions of 4,4,14α-trimethyl-5α-cholesta-8,24-dien-3α-yl and -3β-yl toluene-*p*-sulphonates, 3295.

**Banfield,** J. E. Heterocyclic derivatives of guanidine. Part II. Some derived products. Part III. Stoicheiometry and kinetics of the condensation of ethyl cyanoacetate with guanidino-2*H*-pyrroles. Part IV, 2098, 4332, 4672.

**Banks,** B. E. C. Oxaloacetic acid. Part I. The nature of oxaloacetic acid in the solid state and in neutral, aqueous solution, 5043.

**Banks,** B. E. C., **Diamantis,** A. A., and **Vernon,** C. A. Transamination. Part II. The non-enzymic reactions between pyridoxamine and pyruvic acid and between pyridoxal and alanine, 4235.

**Banks,** B. E. C., **Meinwald,** Y., **Rhind-Tutt,** A. J., **Sheft,** I., and **Vernon,** C. A. Mechanism of reactions in the sugar series. Part IV. The structure of the carbonium ions formed in the acid-catalysed solvolysis of glucopyranosides, 3240.

**Banks,** B. E. C., and **Vernon,** C. A. Transamination. Part I. The isolation of the apoenzyme of glutamic–aspartic transaminase from pig heart muscle, 1698.

**Banks,** R. E., **Ginsberg,** A. E., and **Haszeldine,** R. N. Heterocyclic polyfluoro-compounds. Part I. Pentafluoropyridine, 1740.

**Barben,** I. K. Some substituted ferrocenes, 1827.

**Barber,** H. J., **Washbourn,** K., **Wragg,** W. R., and **Lunt,** E. A new cinnoline synthesis. Part I. Cyclisation of mesoxalyl chloride phenylhydrazones to give substituted 4-hydroxycinnoline-3-carboxylic acids, 2828.

**Barber,** M., **Linnett,** J. W., and **Taylor,** N. H. The halides of the transition elements of the first long period, 3323.

**Barber,** M. S., **Hardisson,** A., **Jackman,** L. M., and **Weedon,** B. C. L. Studies in nuclear magnetic resonance. Part IV. Stereochemistry of the bixins, 1625.

**Barber,** M. S., **Jackman,** L. M., **Warren,** C. K., and **Weedon,** B. C. L. Carotenoids and related compounds. Part IX. The structures of capsanthin and capsorubin, 4019.

**Barbour,** A. K., **Buxton,** M. W., **Coe,** P. L., **Stephens,** R., and **Tatlow,** J. C. Aromatic polyfluoro-compounds. Part VIII. Pentafluorobenzaldehyde and related pentafluorophenyl ketones and carboxylic acids, 808.

**Barclay,** G. A., and **Barnard,** A. K. Complexes of transition metals with a tetra-tertiary arsine, 4269.

**Barclay,** G. A., and **Kennard,** C. H. L. The crystal structure of anhydrous copper(II) formate, 3289.

The crystal structure of monopyridinecopper(II) acetate, 5244.

**Barclay,** G. A., **Nyholm,** R. S., and **Parish,** R. V. Tritertiary arsine complexes of nickel, palladium, and platinum, 4433.

**Barker,** C. C., **Bridge,** M. H., **Hallas,** G., and **Stamp,** A. Steric effects in di- and tri-arylmethanes. Part III. Electronic absorption spectra of derivatives of Malachite Green containing substituents in the phenyl ring, 1285.

**Barker,** C. C., and **Hallas,** G. Steric effects in di- and tri-arylmethanes. Part IV. Electronic absorption spectra of α-alkyl derivatives of Michler's Hydrol Blue. Part V. Electronic absorption spectra of derivatives of Malachite Green containing *ortho*-substituents in the dimethylaminophenyl groups. Part VI. Nucleophilic replacements in triphenylmethane dyes, 1395, 1529, 2642.

**Barker,** C. C., and **Stamp,** A. Steric effects in di- and tri-arylmethanes. Part VII. Biphenyl analogues of Crystal Violet and Malachite Green, 3445.

**Barker**, S. A., **Brimacombe**, J. S., **Harnden**, M. R., and **Stacey**, M. Silyl ethers of tetrahydro-2-hydroxymethylpyran, 5256.

**Barker**, S. A., **Stacey**, M., and **Stroud**, D. B. E. Enzymic synthesis of a glucoxylan, 3995.

**Barker**, S. A. See also **Bailey**, A. J., 4086.

**Barlow**, G. B., and **Clamp**, A. C. Molecular complexes based on derivatives of 4,4′-dihydroxytriphenylmethane, 393.

**Barltrop**, J. A., **Day**, A. C., and **Bigley**, D. B. The reaction of cyanogen chloride with sodium salts of carboxylic acids, 3185.

**Barltrop**, J. A. See also **Acheson**, R. M., 650.

**Barnard**, A. K. See **Barclay**, G. A., 4269.

**Barnard**, D., **Bateman**, L., **Cain**, M. E., **Colclough**, T., and **Cunneen**, J. I. The oxidation of organic sulphides. Part X. The co-oxidation of sulphides and olefins, 5339.

**Barnard**, D., and **Woodbridge**, D. T. Derivatives of *NN*-dialkyldiselenocarbamic acids, 2922.

**Barnard**, P. W. C., **Bunton**, C. A., **Llewellyn**, D. R., **Vernon**, C. A., and **Welch**, V. A. The reactions of organic phosphates. Part V. The hydrolysis of triphenyl and trimethyl phosphates, 2670.

**Barnes**, T. J., and **Hickinbottom**, W. J. 4-Nitro-2,6-di-t-butylphenol and its thermal decomposition, 953.

Molecular rearrangements. Part VI. The thermal rearrangement of *N*-methyl-*N*-*p*-nitrophenylnitramine, 2616.

**Barr**, D. A., **Haszeldine**, R. N., and **Willis**, C. J. Perfluoroalkyl derivatives of nitrogen. Part IX. The reaction of trifluoronitrosomethane with some unsymmetrical olefins, 1351.

**Barraclough**, C. G., **Bradley**, D. C., **Lewis**, J., and **Thomas**, I. M. The infrared spectra of some metal alkoxides, trialkylsilyloxides, and related silanols, 2601.

**Barraclough**, C. G., **Lewis**, J., and **Nyholm**, R. S. Solvent shifts in the infrared spectra of metal carbonyls and their derivatives, 2582.

**Barraclough**, C. G., and **Tobe**, M. L. The preparation and properties of chelated sulphatobis(ethylenediamine)cobalt(III) salts, 1993.

**Barrer**, R. M., and **Denny**, P. J. Hydrothermal chemistry of the silicates. Part IX. Nitrogenous aluminosilicates. Part X. A partial study of the field $CaO$–$Al_2O_3$–$SiO_2$–$H_2O$, 971, 983.

**Barrer**, R. M., and **Perry**, G. S. Sorption of mixtures, and selectivity in alkylammonium montmorillonites. Part I. Monomethylammonium bentonite. Part II. Tetramethylammonium montmorillonite, 842, 850.

**Barrett**, G. C. See **Arcus**, C. L., 1408.

**Barrett**, P. A., **Caldwell**, A. G., and **Walls**, L. P. 6-Methoxy-8-(ω-piperazin-1′-ylalkylamino)quinolines, 2404.

**Barry**, W. J. Sulphonation of arylpyrazoles. Part I. Monosulphonation products of 3-methyl-1,5-diphenylpyrazole, 3851.

**Bartlett**, N., and **Quail**, J. W. The preparation of palladium difluoride and complex fluorides of palladium in selenium tetrafluoride, 3728.

**Bartlett**, N., and **Robinson**, P. L. Co-ordination compounds formed by tetrafluorides of the sulphur sub-group, 3417. Fluorination of the trioxides of chromium, molybdenum, tungsten, and uranium by selenium tetrafluoride, 3549.

**Barton**, D. H. R., **Cheung**, H. T., **Cross**, A. D., **Jackman**, L. M., and **Martin-Smith**, M. Diterpenoid bitter principles. Part III. The constitution of clerodin, 5061.

**Barton**, D. H. R., **McGhie**, J. F., and **Rosenberger**, M. The photoisomerisation of 3β-acetoxylanosta-5,8-dien-7-one, 1215.

**Barton**, D. H. R., **McMorris**, T. C., and **Segovia**, R. The nature of the Porter–Silber reaction, 2027.

**Barton**, D. H. R., **Pradham**, S. K., **Sternhell**, S., and **Templeton**, J. F. Triterpenoids. Part XXV. The constitutions of limonin and related bitter principles, 255.

**Barton**, D. H. R. See also **Autrey**, R. L., 3313.

**Barton**, J. W. See **Baker**, W., 3986.

**Basolo**, F., **Chatt**, J., **Gray**, H. B., **Pearson**, R. G., and **Shaw**, B. L. Kinetics of the reaction of alkyl and aryl compounds of the nickel group with pyridine, 2207.

**Bateman**, L. See **Barnard**, D., 5339.

**Batey**, W., and **Trenwith**, A. B. The thermal decomposition of hexafluoroacetone, 1388.

**Battersby**, A. R., **Davidson**, G. C., and **Turner**, J. C. Ipecacuanha alkaloids. Part VII. The structure of emetamine: stereospecific synthesis of (±)-emetamine and indole analogues of the Ipecacuanha alkaloids, 3899.

**Battersby**, A. R., and **Greenock**, I. A. *cis*- and *trans*-3,3′,4,4′-Tetramethoxystilbenes, 2592.

**Battersby**, A. R., and **Reynolds**, J. J. Studies on specific chemical fission of peptide links. Part III. Fission of peptides containing one glutamic acid residue, 524.

**Baughan**, E. L. See **Davies**, A. G., 1711.

**Bayles**, J. W., and **Taylor**, A. F. The acid–base function in non-aqueous solution. Part II. The equilibria of mono-, di-, and tri-n-butylamine with 2,4-dinitrophenol in several aprotic solvents, 417.

**Bayley**, C. R., **Brammer**, K. W., and **Jones**, A. S. The nucleotide sequence in deoxyribonucleic acids. Part V. The alkaline degradation of apurinic acids, 1903.

**Bayliss**, G. S. See **Armitage**, R., 1842.

**Beaton**, J. M. See **Allison**, J. M., 5224.

**Beattie**, I. R., and **Gilson**, T. The occurrence of organotin cations, 2585.

**Beattie**, I. R., and **Leigh**, G. J. The 2 : 1 addition compound of pyridine with silicon tetranitrate, and related compounds, 4249.

**Beattie**, I. R., and **Vosper**, A. J. Dinitrogen trioxide. Part IV. Composition of the vapour in equilibrium with liquid mixtures of nitrogen dioxide and nitric oxide, 2106.

**Beattie**, I. R., and **Webster**, M. The interaction of phosphorus pentachloride with tertiary amines, 1730.

**Beaven**, G. H., **de la Mare**, P. B. D., **Hassan**, M., **Johnson**, E. A., and **Klassen**, N. V. The kinetics and mechanisms of aromatic halogen substitution. Part X. Products in the chlorination of biphenyl in acetic acid, 2749.

**Beck**, A. See **Kertes**, A. S., 1921, 1926, 5046.

**Beckett**, A. H., and **Lingard**, R. G. Some isomeric amido- and amino-derivatives of 9-methyl- and 9,10-dimethylanthracene, 588.

**Beckwith**, A. L. J. Hydroxylation of 5α,6β-dibromocholestan-3β-yl acetate by chromic acid, 3162.

**Beckwith**, A. L. J., and **See**, L. B. Thiyl radicals. Part I. Reactions of anthracene with oxygen and thiols, 1304.

**Beckwith**, A. L. J., and **Thompson**, M. J. Free-radical phenylation of phenanthrene, 73.

**Beek**, H. C. A. van. See **Heertjes**, P. M., 2148.

**Belcher**, R., **Hoyle**, W., and **West**, T. S. The synthesis of chelating agents related to cyclohexene-1,2-diamine-*NN′N′*-tetra-acetic acid, 667.

**Belcher**, R., **Sobotka**, M., and **Stephen**, W. I. Submicro methods for the analysis of organic compounds. Part XIII. The cryoscopic determination of molecular weight, 480.

**Belič**, I., **Bergant-Dolar**, J., and **Morton**, R. A. Constituents of *Vitex agnus castus* seeds. Part I. Casticin, 2523.

**Bell**, F. 1,2-Quinones from derivatives of 2,7-dihydroxynaphthalene, 5293.

**Bell**, F., and **Gorrie**, J. R. Some derivatives of 2,7-dihydroxynaphthalene, 4258.

**Bell**, F. See also **Anderson**, D. M. W., 4705.

**Bell**, R. P., and **Ford-Smith**, M. H. Kinetics of the alkaline hydrolysis and bromination of bromoform, 1413.

**Bell**, R. P., and **Rawlinson**, D. J. Kinetics of the bromination of some anisoles and phenols, 63.

Kinetics of the bromination of ethyl malonate and methyl methanetricarboxylate, 726.

**Bell**, T. N. Mechanism of the addition of trifluoroiodomethane to ethylene, 4973.

**Bellamy**, L. J., **Eglinton**, G., and **Morman**, J. F. The association of *ortho*-substituted phenols with ethers, 4762.

**Bender**, V. See **Angyal**, S. J., 4718.

**Benn**, M. H., **Creighton**, A. M., **Owen**, L. N., and **White**, G. F. Cytotoxic compounds. Part II. Some amides of the "nitrogen mustard" type, 2365.

**Bennett**, J. E., and **Skinner**, H. A. Thermochemistry of organoboron compounds. Part VI. The heats of reaction of diborane with olefins, 2472.

**Bennett**, M. A., **Pratt**, L., and **Wilkinson**, G. Transition metal complexes of seven-membered ring systems. Part IV. Proton resonance spectra of cycloheptatriene complexes of Group VI metals, 2037.

**Bennett**, M. A., and **Wilkinson**, G. Some observations on rhodium–olefin complexes, 1418.
**Benoiton**, L. An enzymic resolution of serine, 763.
**Bentley**, K. W., and **Dyke**, S. F. Some experiments based on veratraldehyde, 3151.
**Bentov**, M. See **Pelchowicz**, Z., 5418.
**Barcés**, T., and **Trotman-Dickenson**, A. F. The reactions of methoxyl radicals with cyclopropane and isobutane, 348.
The reactions of hydroxyl radicals with hydrocarbons in aqueous solution, 4281.
**Berg**, S. S. A search for new trypanocides. Part VI. Amidinophenyldiazoamino-quinolinium and -quinazolinium salts, 4041.
The search for chemotherapeutic amidines. Part XIX. 3,3′-Diamidinocarbanilide and its congeners, 5097.
**Berg**, S. S., and **Parnell**, E. W. Bisquaternary salts related to quinapyramine (antrycide). Replacement of the quinoline nucleus by other heterocycles, 5275.
**Bergant-Dolar**, J. See **Belič**, I., 2523.
**Bergel**, F., and **Butler**, J. Interaction between carbonyl groups and biologically essential substituents. Part II. Further observations on the effect of ketones on optically active α- and β-amino-esters, 4047.
**Bergel**, F., and **Harrap**, K. R. Interaction between carbonyl groups and biologically essential substituents. Part III. The formation of a thiazolidine derivative in aqueous solution from pyridoxal phosphate and L-cysteine, 4051.
**Bergmann**, E. D., and **Cohen**, S. Organic fluorine compounds. Part XXII. Fluorine analogues of mevalonic acid. Part XXIII. Methylene reactivity in ethyl fluoroacetate. Part XXVI. Synthesis of α-fluoro-β-alanine, 3457, 3537, 4669.
**Bergmann**, E. D., **Cohen**, S., **Hoffman**, E., and **Randmeir**, Z. Organic fluorine compounds. Part XXI. α-Fluorinated keto-compounds, 3452.
**Bergmann**, E. D., **Cohen**, S., and **Shahak**, I. Organic fluorine compounds. Part XX. Some reactions of 1-chloro-3-fluoropropan-2-ol and epifluorohydrin, 3448.
**Bergmann**, E. D., and **Shahak**, I. Organic fluorine compounds. Part XXV. Further reaction of aldehydes with diethyl fluoro-oxaloacetate, 4033.
**Bergmann**, E. D. See also **Pelchowicz**, Z., 4348.
**Bergmann**, F., and **Tamari**, M. The synthesis of 8-substituted purines, 4468.
**Bergmann**, F. See also **Kalmus**, A., 760.
**Bethell**, J. R., and **Maitland**, P. Organic reactions in aqueous solution at room temperature. Part II. The influence of pH on condensations involving the linking of carbon to carbon, of carbon to nitrogen, and of carbon to sulphur, 5211.
**Betts**, B. E., and **Davey**, W. Cyclohexane-1,3-diones. Part V. Reaction of 3-methoxy-2,5-diphenylcyclohex-2-en-1-one with acetone cyanohydrin. Part VI. Structural requirements for the displacement of the alkoxyl by the cyano-group in the enol ethers of cyclic β-diketones. Part VII. Reaction of 3-methoxy-2,4-diphenylcyclohex-2-en-1-one with acetone cyanohydrin, 1683, 3333, 3340.
**Bevan**, C. W. L., **Birch**, A. J., and **Caswell**, H. An insect repellant from black cocktail ants, 488.
**Bevan**, C. W. L. See also **Akisanya**, A., 3705.
**Bews**, A. M. See **Anderson**, D. M. W., 5230.
**Bick**, I. R. C., **Harley-Mason**, J., **Sheppard**, N., and **Vernengo**, M. J. Structural correlations in the nuclear magnetic resonance spectra of bisbenzylisoquinoline and aporphine alkaloids, 1896.
**Bickel**, A. F. See **Zeelenberg**, 4014.
**Biddulph**, R. H., **Brown**, M. P., **Cass**, R. C., **Long**, R., and **Silver**, H. B. Preparation and infrared spectra of trimeric dialkylphosphinoborines and some *B*-halogenated derivatives, 1822.
**Bien**, S. See **Kimchi**, D., 5345.
**Biggs**, A. I. The heat of ionization of some substituted anilines, 2572.
**Biggs**, A. I., and **Robinson**, R. A. The ionisation constants of some substituted anilines and phenols: a test of the Hammett relation, 388.
**Biggs**, J., and **Sykes**, P. 6-Methylthiamine chloride hydrochloride, 2595.
**Bigley**, D. B. See **Barltrop**, J. A., 3185.
**Billing**, C. J., and **Norman**, R. O. C. The *ortho* : *para*-ratio in aromatic substitution. Part IV. The nitration of biphenyl, 3885.
**Birch**, A. J., **Blance**, G. E., **David**, S., and **Smith**, H. Studies in relation to biosynthesis. Part XXIV. Some remarks on the structure of echinulin, 3128.
**Birch**, A. J., **Cameron**, D. W., **Harada**, Y., and **Rickards**, R. W. The structure of the antimycin-A complex, 889.
**Birch**, A. J., and **Grimshaw**, J. Loganin. Part II. Structural interpretation of the spectral properties, 1407.
**Birch**, A. J., **Grimshaw**, J., and **Juneja**, H. R. Aucubin, 5194.
**Birch**, A. J., **Grimshaw**, J., **Penfold**, A. R., **Sheppard**, N., and **Speake**, R. N. An independent confirmation of the structure of geijerene by physical methods, 2286.
**Birch**, A. J., and **Moye**, C. J. The synthesis of 4,5,7-trimethoxy-2-propylanthraquinone, 4691.
**Birch**, A. J., **Shoukry**, E. M. A., and **Stansfield**, F. The base-catalysed isomerisation of some 3-alkyldihydroanisoles, 5376.
**Birch**, A. J., and **Slaytor**, M. The synthesis of (±)-*S*-3-methylbut-2-enylhomocysteine, 4692.
**Birch**, A. J. See also **Bevan**, C. W. L., 488.
**Birchall**, J. M., and **Haszeldine**, R. N. Polyfluoroarenes. Part IV. 2,3,4,5,6-Pentafluorotoluene and related compounds, 3719.
**Birchall**, J. M., **Haszeldine**, R. N., and **Parkinson**, A. R. Polyfluoroarenes. Part III. A new synthesis of hexafluorobenzene, 2204.
**Bird**, C. W., **Cookson**, R. C., and **Crundwell**, E. Cyclisations and rearrangements in the isodrin–aldrin series, 4809.
**Birnbaum**, H., **Cookson**, R. C., and **Lewin**, N. Absorption spectra of ketones. Part VI. Intramolecular charge-transfer spectra, and further examples of intensified $n \longrightarrow \pi^*$ transitions, 1224.
**Blackwell**, J., and **Hickinbottom**, W. J. The reduction of diaryl ketones and diarylmethanols to diarylmethanes, 1405.
**Bladon**, P., and **McMeekin**, W. Steroids derived from hecogenin. Part II. Some ring c-seco-derivatives, 3504.
**Blake**, D., **Coates**, G. E., and **Tate**, J. M. Some reactions of tributyl- and triphenyl-stannyl derivatives of alkali metals, 618.
8-Hydroxyquinoline complexes of the dibutyl- and diphenyl-tin radicals, 756.
**Blakely**, C. F., **Gillespie**, R. J., **Roubinek**, L., **Wassermann**, A., and **White**, R. F. M. Conversion of cyclopentadiene into new bicyclopentyl derivatives; structure determination with the help of proton magnetic resonance spectroscopy, 1939.
**Blakely**, C. F., and **Wassermann**, A. Kinetics and mechanism of the formation of a novel bicyclopentyl derivative: rôle of carbonium ions in the reaction between cyclopentadiene and trichloroacetic acid, 1946.
**Blance**, G. E. See **Birch**, A. J., 3128.
**Bleazard**, W., and **Rothstein**, E. The reaction between aromatic compounds and derivatives of tertiary acids. Part XII. Friedel–Crafts reactions of camphoric anhydride in anisole and in benzene, 68.
**Block**, H. See **Bamford**, C. H., 2057, 4989, 4992.
**Bognár**, R., **Nánási**, P., and **Puskás**, M. Paper-chromatographic investigation of the transglycosylation of *N*-arylhexosylamines and arylamines, 320.
**Bognár**, R. See also **Nánási**, P., 323.
**Bohemen**, J., and **Purnell**, J. H. Diffusional band spreading in gas-chromatographic columns. Part I. The elution of unsorbed gases. Part II. The elution of sorbed vapours, 360, 2630.
**Bokadia**, M. M., **Brown**, B. R., **Kolker**, P. L., **Love**, C. W., **Newbould**, J., **Somerfield**, G. A., and **Wood**, P. M. Polymerisation of flavans. Part V. The stereochemistry of 2,3-*trans*-flavan-3,4-diols, 4663.
**Bolton**, C. H., **Foster**, A. B., **Stacey**, M., and **Webber**, J. M. Carbohydrate components of antibiotics. Part I. Degradation of desosamine by alkali: its absolute configuration at position 5, 4831.
**Boocock**, J. R. B., and **Hickinbottom**, W. J. The synthesis and reactions of branched-chain hydrocarbons. Part XIV. The free-radical halogenation of t-butylbenzene, 2587.

XUM

**Booth**, D. H., and **Coates**, R. V. The stability of calcium hydrogen phosphate precipitated from solutions of calcium nitrate and phosphoric acid, 4914.
**Bottomley**, G. A., and **Coopes**, I. H. Nitromethane: second virial coefficients, 2247.
**Bourne**, E. J., **Burdon**, J., **McLoughlin**, V. C. R., and **Tatlow**, J. C. Studies of trifluoroacetic acid. Part XVIII. Reaction of *N*-aroylglycines with perfluoro-carboxylic anhydrides, 1771.
**Bourne**, E. J., **Hartigan**, J., and **Weigel**, H. Biosynthesis of α-D-glucopyranosyl D-galactofuranoside and other D-galactose-containing saccharides by *Betacoccus arabinosaceus*, 1088.
**Bourne**, E. J., **Hutson**, D. H., and **Weigel**, H. Complexes between molybdate and acyclic polyhydroxy-compounds, 35.
**Bourne**, E. J. See also **De Belder**, A. N., 4464.
**Boutle**, D. L., and **Bunton**, C. A. Deamination of cyclohexylamine by [$^{18}$O]nitrous acid, 761.
**Bowers**, A., **Denot**, E., **Sanchez**, M. B., **Neumann**, F., and **Djerassi**, C. Steroidal sapogenins. Part XI. Reaction of 12-oxo-sapogenins with selenium dioxide: synthesis of 3β-hydroxypregna-5,9(11),16-trien-20-one from botogenin, 1859.
**Bowers**, A., **Holton**, P. G., **Necoechea**, E., and **Kincl**, F. A. Steroids. Part CLXIX. The preparation of 16α-methyl- and 16β-methyl-testosterone, 4057.
**Boyland**, E., and **Nery**, R. The reaction between *N*-methyldi(2-chloroethyl)amine and thiosulphate, 679.
**Braddock**, J. M. F., and **Coates**, G. E. Arsinophosphonium salts, 3208.
**Bradley**, D. C. See **Barraclough**, C. G., 2601.
**Bradley**, J. N., and **Ledwith**, A. The reactions of carbene with alkyl halides, 1495.
**Bragg**, D. R., and **Wibberley**, D. G. Condensation of ethyl 2- and 4-pyridylacetate with aromatic carbonyl compounds, 5074.
**Brain**, E. G., **Doyle**, F. P., and **Mehta**, M. D. Pharmacodynamic compounds. Part II. Some rearrangements in the pyrrolidine–piperidine series, 633.
**Brammer**, K. W. See **Bayley**, C. R., 1903.
**Brandon**, R. W., and **Lucken**, E. A. C. The electron-spin resonance spectra and odd-electron distribution of a number of polycyclic semiquinones and their derivatives, 4273.
**Braude**, G. L., and **Cogliano**, J. A. Kinetics of the reaction between chloramine and tertiary amines, 4172.
**Bretherick**, L., **Gaimster**, K., and **Wragg**, W. R. A convenient alternative synthesis of 5-hydroxytryptamine, 2919.
**Brewis**, S., and **Halsall**, T. G. The chemistry of triterpenes and related compounds. Part XXXVIII. The acidic constituent of dammar resin, 646.
**Brewis**, S. See also **Bacon**, N., 2255.
**Brewster**, J. A., **Savage**, C. A., and **Venanzi**, L. M. Some five-co-ordinate complexes of platinum(II), 3699.
**Bridge**, M. H. See **Barker**, C. C., 1285.
**Briggs**, L. H., and **Cazabie**, R. C. Constituents of *Eugenia maire* A. Cunn. Part II. Identification of mairin and constituents of the leaves, 4684.
**Briggs**, L. H., **Cambie**, R. C., and **Hoare**, J. L. *Solanum* alkaloids. Part XV. The constituents of some *Solanum* species and a reassessment of solasodamine and solauricine, 4645.
**Briggs**, L. H., **Cambie**, R. C., **Lowry**, J. B., and **Seelye**, R. N. Constituents of *Eugenia maire* A. Cunn. Part I. A trimethyl ether of ellagic acid and mairin, a new triperpene, 642.
**Brimacombe**, D. A. See **Norman**, R. O. C., 3247.
**Brimacombe**, J. S. See **Barker**, S. A., 5256.
**Brittain**, E. F., **Kohnstam**, G., **Queen**, A., and **Shillaker**, B. Activation parameters for $S_N1$ solvolysis in 50% aqueous acetone 2045.
**Bromberger**, B., and **Phillips**, L. The abstraction of nitric oxide from alkyl nitrites in the vapour phase by methyl radicals, 5302.
**Brook**, A. J. See **Allen**, C. R., 2171.
**Brooke**, G. M., **Burdon**, J., and **Tatlow**, J. C. Aromatic polyfluoro-compounds. Part VII. The reaction of pentafluoronitrobenzene with ammonia, 802.
**Brookes**, P., and **Lawley**, P. D. The alkylation of guanosine and guanylic acid, 3923.
**Brooks**, C. J. W., **Eglinton**, G., and **Magrill**, D. S. The constitution of an oxidation product of β-ionone, 308.
**Brooks**, C. J. W., **Eglinton**, G., and **Morman**, J. F. Infrared spectra of aryl carboxylic acids and their esters, 106. Infrared spectra of substituted salicylic acids and their esters, 661.
**Brooks**, C. J. W., and **Morman**, J. F. Infrared spectra of substituted salicylaldehydes, 3372.
**Brooks**, G. T. See **Ansell**, M. F., 201, 212.
**Brown**, B. R., **Cummings**, W., and **Newbould**, J. Polymerisation of flavans. Part IV. The condensation of flavan-4-ols with phenols, 3677.
**Brown**, B. R., **Trown**, P. W., and **Woodhouse**, J. M. 4-Substituted steroids derived by rearrangement and reduction of cholestenone enol acetate, 2478.
**Brown**, B. R. See also **Bokadia**, M. M., 4663.
**Brown**, D., and **Wilkins**, R. G. Further observations on the absorption spectra of protactinium-(IV) and -(V) in certain solutions, 3804.
**Brown**, D. A. The variation of bond type in cyclopentadienyl–metal compounds, 690.
**Brown**, D. H. Tungstate and molybdate complexes with glycollic and mandelic acid, 4732.
**Brown**, D. H. See also **Baillie**, M. J., 3691.
**Brown**, D. J., and **Harper**, J. S. Pyrimidine reactions. Part III. The methylation product of 4-amino-6-hydroxypyrimidine, and related compounds, 1298.
**Brown**, D. J., and **Jacobson**, N. W. Pteridine studies. Part XIV. Methylation of 2-amino-4-hydroxypteridine and related compounds, 4413.
**Brown**, D. M., **Clark**, B. F. C., and **Letters**, R. Phospholipids. Part VII. The structure of a monophosphoinositide, 3774.
**Brown**, D. N., **Hey**, D. H., and **Rees**, C. W. Internuclear cyclisation. Part XVII. The independent synthesis of some *N*-methylbenzophenanthridones and their formation by internuclear cyclisation, 3873.
**Brown**, M. P. See **Biddulph**, R. H., 1822.
**Brown**, R. J., **Carver**, F. W. S., and **Hollingsworth**, B. L. The reaction of ethyl 2-oxocyclopentanecarboxylate with arylamines. Part I. The preparation of 2,3-dihydro-α-quinindones (2,3,4,5-tetrahydro-4-oxo-1*H*-cyclopenta[*c*]quinolines), 4295.
**Brown**, S. S., and **Timmis**, G. M. The preparation of αω-di-*O*-methanesulphonyl derivatives of some sugar alcohols, 3656.
**Browne**, G. F., **Johns**, R. B., and **Markham**, K. R. Picrotoxin and tutin. Part XI, 3000.
**Browning**, M. C., **Davies**, R. F. B., **Morgan**, D. J., **Sutton**, L. E., and **Venanzi**, L. M. Tetrahedral nickel(II) complexes and the factors determining their formation. Part III. Complexes with triarylphosphines, 4816.
**Brukson**, S. See **Pelchowicz**, Z., 4348.
**Bryce-Smith**, D., and **Cox**, G. F. Organometallic compounds of Group II. Part III. Unsolvated organomagnesium halides, 1175.
**Bryce-Smith**, D., and **Perkins**, N. A. Tropylium complex halide salts of boron, aluminium, iron, titanium, and tin, 2320.
**Buchanan**, J. G. See **Baddiley**, J., 2180.
**Büchi**, G., **Crombie**, L., **Godin**, P. J., **Kaltenbronn**, J. S., **Siddalingaiah**, K. S., and **Whiting**, D. A. The absolute configuration of rotenone, 2843.
**Buchner**, P., **Cooper**, R. E., and **Wassermann**, A. Influence of counter-ion fixation on molecular weight and shape of polyelectrolyte, 3974.
**Buck**, K. W., **Foster**, A. B., **Richtmyer**, N. K., and **Zissis**, Aspects of stereochemistry. Part VII. The structure of some cyclic acetals of D-*glycero*-D-*gluco*-heptitol (β-sedoheptitol), 3633.
**Buckingham**, A. D., and **Raab**, R. E. The dielectric polarisation of some imperfect polar gases, 5511.
**Buffagni**, S., and **Dunn**, T. M. The spectra of inorganic complexes in non-aqueous solvents. Part I. Chloride, cobaltate ion and cobalt chloride, 5105.
**Bu'Lock**, J. D. The formation of melanin from adrenochrome, 52.

**Bu'Lock**, J. D., **Allport**, D. C., and **Turner**, W. B. The biosynthesis of polyacetylenes. Part III. Polyacetylenes and triterpenes in *Polyporus anthracophilus*, 1654.
**Bu'Lock**, J. D., **Gregory**, H., and **Hay**, M. The biosynthesis of polyacetylenes. Part IV. The rate of polyacetylene synthesis by Basidiomycete B.841, 3544.
**Bunton**, C. A., and **Hadwick**, T. Tracer studies in ester hydrolysis. Part IX. Phenyl and diphenylmethyl trifluoroacetate, 943.
**Bunton**, C. A., **Llewellyn**, D. R., **Vernon**, C. A., and **Welch**, V. A. The reactions of organic phosphates. Part IV. Oxygen exchange between water and orthophosphoric acid, 1636.
**Bunton**, C. A. See also **Armour**, C., 412, **Barnard**, P. W. C., 2670, and **Boutle**, D. L., 761.
**Burdon**, J., **Smith**, T. J., and **Tatlow**, J. C. Cyanohydrins of ethyl γγγ-trifluoroacetoacetate and 5,5,5-trifluoro-4-oxopentanoic acid, 4519.
**Burdon**, J. See also **Bourne**, E. J., 1771, and **Brooke**, G. M., 802.
**Burgess**, A. R., and **Cullis**, C. F. The gaseous oxidation of isopropyl alcohol. Part II. Influence of the surface on the formation of hydrogen peroxide and other products, 3041.
**Burgess**, A. R., **Cullis**, C. F., and **Newitt**, E. J. The gaseous oxidation of isopropyl alcohol. Part I. The influence of temperature, pressure, and mixture composition on the formation of hydrogen peroxide and other products, 1884.
**Burn**, A. J., and **Cadogan**, J. I. G. The reactivity of organophosphorus compounds. Part IX. The reaction of thionates with alkyl iodides, 5532.
**Burn**, A. J., **Cadogan**, J. I. G., and **Moulden**, H. N. The reactivity of organophosphorus compounds. Part X. The reaction of phosphorothiolates with alkyl iodides, 5542.
**Burrows**, B. F. See **Baker**, W., 2257.
**Burton**, R., **Pratt**, L., and **Wilkinson**, G. Transition-metal complexes of seven-membered ring systems. Part III. Cycloheptatrieneiron carbonyl and related compounds, 594.
**Butler**, A. R., and **Gold**, V. The hydrolysis of acetic anhydride. Part VI. Kinetics in deuterium oxide solution. Part VII. Catalysis by pyridine and methylpyridines in acetate buffers, 2305, 4362.
**Butler**, D. N. See **Naylor**, R. N., 4845.
**Butler**, J. See **Bergel**, F., 4047.
**Bau-Hoï**, N. P., **Jacquignon**, P., and **Allegrini**, E. Carcinogenic nitrogen compounds. Part XXXI. Benzacridines and other nitrogen-heterocyclic derivatives of *m*-ethylaniline, 4836.
**Bau-Hoï**, N. P., and **Saint-Ruf**, G. Carcinogenic nitrogen compounds. Part XXX. 2,3-Dipyridylquinoxalines and 5,6-dipyridylpyrido(2′,3′-2,3)pyrazines, 2258.
**Bau-Hoï**, N. P. See also **Mabille**, P., 4911, and **Marty**, M., 384.
**Buxton**, M. W. See **Barbour**, A. K., 808.

## C

**Cadogan**, J. I. G. The reactivity of organophosphorus compounds. Part IV. The reaction of carbonyl chloride with some esters, 3067.
**Cadogan**, J. I. G., and **Foster**, W. R. The reactivity of organophosphorus compounds. Part V. The reaction of trichloromethyl radicals with trialkyl phosphites. Part VI. *N*-Chloroamidates, 3071, 3076.
**Cadogan**, J. I. G., **Hey**, D. H., and **Sanderson**, W. A. Organic peroxides. Part V. The decomposition of di-(9-phenyl-9-fluorenyl) peroxide. Part VI. The decomposition of *p*-nitrophenyldiphenylmethyl peroxides, 3879, 5236.
**Cadogan**, J. I. G., and **Moulden**, H. N. The reactivity of organophosphorus compounds. Part VII. Reactions between phosphites and chloramine-T. Part VIII. The reactions of chloramine-T with triethyl phosphorothiolate and related compounds, 3079, 5524.
**Cadogan**, J. I. G. See also **Burn**, A. J., 5532, 5542.
**Cady**, G. H., and **Hargreaves**, G. B. The vapour pressures of some heavy transition-metal hexafluorides, 1563.
Vapour pressures of some fluorides and oxyfluorides of molybdenum, tungsten, rhenium, and osmium, 1568.
**Cain**, B. F. Potential anti-tumour agents. Part I. Polyporic acid series, 936.
Tumour inhibitors from plant sources. Part I, 2599.
**Cain**, M. E. See **Barnard**, D., 5339.
**Cairns-Smith**, A. G. Tautomerism in the solid state. Part I. Thermochromism of heterocyclic phenols, 182.
**Cairns-Smith**, A. G. See also **Campbell**, N., 1191.
**Caldin**, E. F. See **Allen**, C. R., 2171.
**Caldwell**, A. G. See **Barrett**, P. A., 2404.
**Cambie**, R. C. See **Briggs**, L. H., 642, 4645, 4684.
**Cameron**, D. W. See **Birch**, A. J., 889.
**Campbell**, I. G. M., and **Way**, J. K. Synthesis and stereochemistry of heterocyclic phosphorus compounds. Part II. Loss of optical activity in the reduction of (+)-2-carboxy-9-phenyl-9-phosphafluorene 9-oxide, 2133.
**Campbell**, N., and **Cairns-Smith**, A. G. Tautomerism in the solid state. Part II, 1191.
**Candlin**, J. P., and **Wilkins**, R. G. Sulphur–nitrogen compounds. Part II. The hydrolysis of hydroxylaminetrisulphonate and hydroxylamine-*NO*-disulphonate ions in perchloric acid, 3625.
**Capon**, B., **Overend**, W. G., and **Sobell**, M. Reactions at position 1 of carbohydrates. Part II. The variation of optical rotation of some aryl glucosides with temperature, 5172.
**Carman**, R. M., and **Grant**, P. K. Biformene, 2187.
**Carrington**, T. R., **Eardley**, S., **Elks**, J., **Green**, G. F. H., **Gregory**, G. I., **Long**, A. G., and **Sly**, J. C. P. Compounds related to the steroid hormones. Part VI. The synthesis of the 9α-fluoro-16β-methyl derivatives of hydrocortisone and prednisolone, 4560.
**Carruthers**, W., **Cook**, J. W., **Glen**, N. A., and **Gunstone**, F. D. Experiments confirming the structure of shellolic acid, 5251.
**Carter**, P., and **Stevens**, T. S. Rearrangement of sulphonhydrazides, 1743.
**Carver**, F. W. S. See **Brown**, R. J., 4295.
**Casapieri**, P., and **Swart**, E. R. Concomitant first- and second-order nucleophilic substitution, 4342.
**Case**, J. R., **Ray**, N. H., and **Roberts**, H. L. Sulphur chloride pentafluoride: reaction with unsaturated hydrocarbons, 2066.
Sulphur chloride pentafluoride: reaction with fluoro-olefines, 2070.
**Casimir**, D. J., **Harle**, A. J., and **Lyons**, L. E. The polarographic reduction of some heterocyclic molecules. Part III. Quinoline ethiodide, 5297.
**Cass**, R. C. See **Biddulph**, R. H., 1822.
**Caswell**, H. See **Bevan**, C. W. L., 488.
**Casy**, A. F. Action of thionyl chloride upon alcohols derived from alpha- and beta-prodine, 5057.
**Cavell**, E. A. S., and **Speed**, J. A. Effect of solvent composition on the kinetics of reactions between ions and dipolar molecules. Part III, 226.
**Chamberland**, B. L., and **MacDiarmid**, A. G. Preparation of monomers and polymers containing Sn–O–As(v) linkages, 445.
**Chambers**, R. D., **Musgrave**, W. K. R., and **Savory**, J. Mixtures of halogens and halogen polyfluorides as effective sources of the halogen monofluorides in reactions with fluoro-olefins, 3779.
**Champion**, N. G. S., **Foster**, R., and **Mackie**, R. K. π-Molecular complex of hexamethylborazole with tetracyanoethylene, 5060.
**Chan**, S. C. See **Baldwin**, M. E., 4637.
**Chang**, C. T., and **Chen**, F. C. Synthesis of 7-fluoroflavone and related compounds, 3155.
**Chang**, C. T., **Chen**, F. C., **Chen**, T. S., **Hsu**, K. K., **Ueng**, T., and **Hung**, M. Synthesis of 6-halogenoflavones and related compounds, 3414.
**Chapman**, A. C., **Holmes**, W. S., **Paddock**, N. L., and **Searle**, H. T. Phosphonitrilic derivatives. Part VI. *N*-Methyltrichlorophosphinimine dimer, 1825.
**Chapman**, A. C., **Paine**, D. H., **Searle**, H. T., **Smith**, D. R., and **White**, R. F. M. Phosphonitrilic derivatives. Part V. The triphosphonitrilic fluoride chlorides, 1768.
**Chapman**, J. H., and **Parker**, A. C. The ultraviolet absorption of isolated double bonds, 2075.

**Chapman**, N. B., **Shorter**, J., and **Toyne**, K. J. Conformation and reactivity. Part III. Kinetics of the acid-catalysed hydrolysis of the methyl cyclohexane-mono- and -di-carboxylates and 4-t-butylcyclohexanecarboxylates, 2543.

**Chapman**, N. B., and **Taylor**, H. Synthesis of *NN*-dialkyl-*N'*-arylalkyl-*N'*-4-quinazolyl(or 6-methyl-4-pyrimidyl or 4-methyl-2-pyrimidyl)ethylenediamines of potential pharmacological interest, 1908.

**Chapman**, N. B., and **Tompsett**, A. J. Di-*N*-substituted 2-halogenoethylamines. Part V. Fluorenylamine, thenylamine, and thionaphthenylmethylamine derivatives: their synthesis, reactivity, and pharmacology, 1291.

**Chapman**, N. B. See also **Allen**, J. F., 1076.

**Charman**, H. B., **Hughes**, E. D., **Ingold**, Sir C., and **Thorpe**, F. G. Mechanism of electrophilic substitution at a saturated carbon atom. Part III. Kinetics, stereochemistry, and mechanism of the three-alkyl mercury-exchange reaction, 1121.

**Charman**, H. B., **Hughes**, E. D., **Ingold**, Sir C., and **Volger**, H. C. Mechanism of electrophilic substitution at a saturated carbon atom. Part V. Kinetics, stereochemistry, and mechanism of anion-catalysed one-alkyl mercury-exchange reactions, 1142.

**Chatt**, J., **Guy**, R. G., and **Duncanson**, L. A. Complexes of acetylenes with platinum(II). Part I. Alkynes, 827.

**Chatt**, J., **Guy**, R. G., and **Watson**, H. R. $\pi$-Complexes of biphenylene, 2332.

**Chatt**, J., and **Hart**, F. A. Thiocyanato-bridged complexes of platinum(II), 1416.

**Chatt**, J., **Hart**, F. A., and **Rosevear**, D. T. The reaction of metals with *o*-phenylenebis(diethylphosphine), 5504.

**Chatt**, J., and **Hayter**, R. G. Ligand field strengths of the halide, methyl, phenyl, and hydride anions, 772.

Some complexes of tertiary phosphines with ruthenium(II) and osmium(II), 896.

Hydrido-complexes of ruthenium(II) and osmium(II), 2605.

Some hydrido-complexes of iron(II), 5507.

**Chatt**, J., and **Shaw**, B. L. Alkyls and aryls of transition metals. Part IV. Cobalt(II) and iron(II) derivatives, 285.

**Chatt**, J., and **Watson**, H. R. The reactions of di- and tri-tertiary phosphines with the hexacarbonyls of metals of Group VI, 4980.

**Chatt**, J. See also **Adams**, D. M., 738, and **Basolo**, F., 2207.

**Chatterjea**, J. N., **Curtis**, R. F., and **Dhoubhadel**, S. P. The synthesis of dinaphtho(2′,3′-2,3)(2″,3″-4,5)furan, 765.

**Chatterjee**, A., and **Chaudhury**, B. The synthesis of bergamottin, 2246.

**Chatterjee**, A., **Srimany**, S. K., and **Chaudhury**, B. The mechanism of hydramine fission, 4576.

**Chaudhry**, G. R., **Halsall**, T. G., and **Jones**, E. R. H. The chemistry of the triterpenes and related compounds. Part XXXIX. Some derivatives of 4,4-dimethylcholestan-3-one, 2725.

**Chaudhury**, B. See **Chatterjee**, A., 2246, 4576.

**Cheeseman**, G. W. H. Quinoxalines and related compounds. Part V. Some experiments with 1,2-dihydro-2-oxoquinoxalines, 1246.

**Cheeseman**, G. W. H., **Katritzky**, A. R., and **Øksne**, S. The infrared spectra of polycyclic heteroaromatic compounds. Part II. Quinoxaline-2,3-diones, 3983.

**Chen**, F. C. See **Chang**, C. T., 3155, 3414.

**Chen**, T. S. See **Chang**, C. T., 3414.

**Cheung**, H. T. See **Barton**, D. H. R., 5061.

**Chia**, L. H. L. See **Aroney**, M., 4144.

**Choguill**, H. S., and **Ridd**, J. H. The mechanism of protodeiodination of *p*-iodoaniline, 822.

**Christensen**, T. B. See **Aspinall**, G. O., 3461.

**Chuchani**, G. Competition between aniline and phenol for a triphenylmethyl cation, 575.

**Ciampolini**, M., **Paoletti**, P., and **Sacconi**, L. Thermochemical studies. Part IV. Heats and entropies of reaction of transition-metal ions with diethylenetriamine, 2994.

**Ciampolini**, M. See also **Sacconi**, L., 5115.

**Clamp**, A. C. See **Barlow**, G. B., 393.

**Clancy**, M. J., and **Turvey**, J. R. Sulphates of monosaccharides and derivatives. Part III. Acid hydrolysis, 2935.

**Clancy**, M. J. See also **Turvey**, J. R., 1692.

**Clark**, B. F. C. See **Brown**, D. M., 3774.

**Clark**, H. C., **Horsfield**, A., and **Symons**, M. C. R. Unstable intermediates. Part XII. The radical-ions $SO_3^-$ and $NO_3^{2-}$, 7.

**Clark**, J., and **Lister**, J. H. A novel cyclisation procedure for the preparation of chloro- and other purines, 5048.

**Clark**, V. M., **Hutchinson**, D. W., **Kirby**, G. W., and **Todd**, Sir A. Studies on phosphorylation. Part XXII. Phosphorylation accompanying the oxidation of quinol phosphates, 715.

**Clark**, V. M., **Hutchinson**, D. W., and **Todd**, Sir A. Studies on phosphorylation. Part XXIII. Oxidative phosphorylation leading to adenosine-5′ pyrophosphate, 722.

**Clark-Lewis**, J. W., **Katekar**, G. F., and **Mortimer**, P. I. Flavan derivatives. Part IV. Teracacidin, a new leucoanthocyanidin from *Acacia intertexta*, 499.

**Clark-Lewis**, J. W., and **Mortimer**, P. I. The 4-hydroxypipecolic acid from *Acacia* species, and its stereoisomers, 189.

Application of Hudson's lactone rule to hydroxypipecolic acids; an anomaly, 4268.

**Clark-Walker**, G. D., and **Robinson**, H. C. A coloured maleimide and its interaction with cysteine, 2810.

**Clifford**, B., **Nixon**, P., **Salt**, C., and **Tomlinson**, M. 4- and 6-Hydroxy-2,3-diphenylindole and 2,3-diphenylindole-4,7- and -6,7-quinone, 3516.

**Clunie**, J. S., and **Robertson**, J. M. The structure of isoclovene: *X*-ray analysis of the hydrochloride and hydrobromide, 4382.

**Coates**, G. E., and **Livingstone**, J. G. Aminodiarylboranes and their phosphorus and arsenic analogues, 1000.

Aminoditolylborane and the preparation of diarylborinic acids, 4909.

Phosphino-arylboranes, 5053.

**Coates**, G. E. See also **Blake**, D., 618, 756, and **Braddock**, J. M. F., 3208.

**Coates**, R. V. See **Booth**, D. H., 4914.

**Cocker**, W., **Hopkins**, L. O., **McMurry**, T. B. H., and **Nisbet**, M. A. Some reduction products of helenin, 4721.

**Coe**, P. L. See **Barbour**, A. K., 808.

**Cogliano**, J. A. See **Braude**, G. L., 4172.

**Cohen**, M. See **Allen**, M. J., 757.

**Cohen**, S. See **Bergmann**, E. D., 3448, 3452, 3457, 3537, 4669.

**Colclough**, T. See **Barnard**, D., 5339.

**Coldrey**, J. M. See **Addison**, C. C., 468.

**Collins**, R. F., and **Davis**, M. The chemotherapy of schistosomiasis. Part IV. Some ethers of 4-amino-2-methoxyphenol, 1863.

**Connett**, J. E. See **Attenburrow**, J., 4547.

**Connolly**, J. D., and **Overton**, K. H. The constitution and stereochemistry of the lactone $C_{10}H_{16}O_4$ formed in the oxidation of camphor by peracids, 3366.

**Cook**, J. W. See **Carruthers**, W., 5251.

**Cookson**, R. C., **Cox**, D. A., and **Hudec**, J. Photodimers of alkylbenzoquinones, 4499.

**Cookson**, R. C. See also **Bird**, C. W., 4809, and **Birnbaum**, H., 1224.

**Cooley**, G., **Ducker**, J. W., **Ellis**, B., **Petrow**, V., and **Scott**, W. P. Modified steroid hormones. Part XXIII. Some pentacyclic types, 4108.

**Coombs**, M. M., and **Houghton**, R. P. Macrocyclic bis-(1,3-diketones), 5015.

**Cooper**, R. E. See **Buchner**, P., 3974, and **Katchalsky**, A., 5198.

**Cooper**, S., **Frazer**, M. J., and **Gerrard**, W. Interaction of boron trichloride with dioxan and 1,3-dioxolan, 5545.

**Coopes**, I. H. See **Bottomley**, G. A., 2247.

**Copeland**, P. G., **Dean**, R. E., and **McNeil**, D. The ozonolysis of polycyclic hydrocarbons. Part II. Part III. Part IV, 1232, 3858, 3864.

**Corbett**, J. F., and **Holt**, P. F. Polycyclic cinnoline derivatives. Part VIII. Cinnolines and their *N*-oxides and *oo'*-diaminobiaryls. Part IX. The bromination of benzo[*c*]cinnoline and the preparation and ultraviolet absorption spectra of reference compounds, 3695, 5029.

The formation of a substituted biphenylene by an Ullmann reaction, 4261.

**Corbett**, J. F., **Holt**, P. F., and **Hughes**, A. N. Polycyclic cinnoline derivatives. Part VI. The ultraviolet absorption of polycyclic cinnolines and their *N*-oxides, 1363.

**Corbett**, W. M. The cross-linking of cellulose and its derivatives. Part II. Preparation of some new amino-derivatives of D-glucose and of D-galactose, 2926.
**Corbett**, W. M., and **Liddle**, A. M. The alkaline degradation of glucose and of some of its acetyl derivatives, 531.
**Corbett**, W. M., and **McKay**, J. E. The cross-linking of cellulose and its derivatives. Part III. The addition of amines to crotonyl esters, 2930.
**Corbett**, W. M., **McKay**, J. E., and **Taylor**, W. The cross-linking of cellulose and its derivatives. Part V. The stability of some *N*-substituted β-aminobutyric acids and their esters, 5041.
**Corbett**, W. M., and **Winters**, D. The cross-linking of cellulose and its derivatives. Part IV. The action of hydrazine on the toluene-*p*-sulphonates of di-*O*-isopropylidene-D-galactose and -D-fructose, 4823.
**Corkill**, J. M., and **Graham-Bryce**, I. J. The luminescence of some substituted naphthalenes, 3893.
**Cort**, L. A. Some derivatives of *S*-(2-hydroxyethyl)thiourea, 5191.
**Cotton**, F. A. See **Francis**, R., 2078, and **Goodgame**, D. M. L., 2298, 3735.
**Coussmaker**, C. R. C., **Hutchinson**, M. H., **Mellor**, J. R., **Sutton**, L. E., and **Venanzi**, L. M. Tetrahedral nickel(II) complexes and the factors determining their formation. Part II. Complexes with dibutylphenylphosphine and butyldiphenylphosphine, 2705.
**Coutts**, R. T., **Hooper**, M., and **Wibberley**, D. G. 1,2-Dihydro-1,4-dihydroxy-2-oxoquinolines preparation by reductive cyclisation with hydrazine hydrate and palladium–charcoal, 5058.
Isatogens. Part I. Base-catalysed condensation products of methyl and ethyl *o*-nitrobenzoylacetate and *o*-nitrobenzoylacetone, 5205.
**Covell**, C. J., **King**, F. E., and **Morgan**, J. W. W. The chemistry of extractives from hardwoods. Part XXXI. 2-Acetyl-1,8-dihydroxy-3-methylnaphthalene (musizin), a constituent of *Maesopsis eminii*, 702.
**Cowley**, B. R., and **Waters**, W. A. Some reactions of the dimethylamino-radical, ·NMe$_2$, 1228.
**Cox**, D. A. See **Cookson**, R. C., 4499.
**Cox**, G. F. See **Bryce-Smith**, D., 1175.
**Cox**, J. J. See **Irving**, H., 1470.
**Coxon**, B., and **Hough**, L. Derivatives of 3-acetamido-3-deoxy-D-altrose and their conversion into 2-acetamido-2-deoxy-D-ribose, 1463.
The eperimerization of 2-acetamido-2-deoxy-D-pentoses, 1577.
3-Acetamido-3-deoxy-D-allose diethyl dithioacetal and its oxidation by peroxypropionic acid, 1643.
**Coyle**, T. D., **Stafford**, S. L., and **Stone**, F. G. A. The nuclear magnetic resonance spectrum of *cis*-1,2-difluoroethylene, 743.
Chemical and spectroscopic evidence for the occurrence of π-character in carbon–boron bonds, 3103.
**Crabtree**, A., **Johnson**, A. W., and **Tebby**, J. C. The reaction of pyridine with methyl propiolate, 3497.
**Craig**, D. P., **Heffernan**, M. L., **Mason**, R., and **Paddock**, N. L. Delocalization and magnetic properties of the phosphonitrilic halides, 1376.
**Craig**, J. C. See **Shoppee**, C. W., 1311, 2291.
**Creighton**, A. M., **Owen**, L. N., and **White**, G. R. Cytotoxic compounds. Part III. Some derivatives of *p*-(*NN*-di-2-chloroethyl- and of *p*-(*NN*-di-2-bromoethyl-amino)thiophenol, 2375.
**Creighton**, A. M. See also **Benn**, M. H., 2365.
**Cremlyn**, R. J. W. Reactions between *O*-benzenesulphonyllactims and phosphates, 1641.
The reaction between acetamidates and acid esters of phosphoric acid, 1805.
Thiophthalimides, 5055.
Thiosuccinimides, 5547.
**Cresswell**, R. M., **Neilson**, T., and **Wood**, H. C. S. Pteridine derivatives. Part VIII. A new synthesis of riboflavin and related isoalloxazines, 476.
**Cresswell**, R. M., **Smith**, W. R. D., and **Wood**, H. C. S. The structure of two trimers of biacetyl, 4882.
**Criddle**, W. J. See **Phillips**, G. O., 3756, 3763.
**Cromartie**, R. I. T., and **Hamied**, Y. K. Ethylidene acetals of cyclohexane-*cis*- and -*trans*-1,2-diol, 3622.
**Cromartie**, R. I. T., and **Murrell**, J. N. Steric effects on the spectra of aromatic hydrocarbons, 2063.
**Cromartie**, R. I. T., and **Scott**, P. M. A new synthesis of isodunniol, 3548.
**Crombie**, L., and **Godin**, P. J. The structure and stereochemistry of the rotenolones, rotenolols, isorotenolones, and isorotenolols, 2861.
**Crombie**, L., **Godin**, P. J., **Whiting**, D. A., and **Siddalingaiah**, K. S. Some chemistry of the B/C-ring system of rotenoids, 2876.
**Crombie**, L., and **Peace**, R. Structure and stereochemistry of sumatrol and malaccol, 5445.
**Crombie**, L. See also **Büchi**, G., 2843.
**Crook**, E. M. See **Keay**, L., 710.
**Cross**, A. D. Seymnol sulphate and anhydroscymnol, 2817.
**Cross**, A. D., **King**, F. E., and **King**, T. J. The chemistry of extractives from hardwoods. Part XXXII. Adifoline, an alkaloid from *Adina cordifolia*, 2714.
**Cross**, A. D. See also **Barton**, D. H. R., 5061.
**Cross**, B., and **Whitham**, G. H. Conformationally fixed olefins. Part III. The stereochemistry of the reaction of t-butyl perbenzoate with 1-methylene-4-t-butylcyclohexane, 1650.
**Cross**, B. E., **Grove**, J. F., and **Morrison**, A. Gibberellic acid. Part XVIII. Some rearrangements of ring A, 2498.
**Crowley**, H. C. See **Mattocks**, A. R., 5400.
**Cruickshank**, D. W. J. The rôle of 3*d*-orbitals in π-bonds between (*a*) silicon, phosphorus, sulphur, or chlorine and (*b*) oxygen or nitrogen, 5486.
**Crunden**, E. W., and **Hudson**, R. F. The mechanism of hydrolysis of acid chlorides. Part VII. Alkyl chloroformates, 3748.
**Crundwell**, E. See **Bird**, C. W., 4809.
**Csepreghy**, G. See **Fodor**, G., 3222.
**Cullinane**, N. M., **Woolhouse**, R. A., and **Edwards**, B. F. R. The Fries rearrangement of *p*-tolyl acetate catalysed by zirconium tetrachloride and stannic chloride, 3842.
**Culling**, G. C. See **Ansell**, M. F., 2908.
**Cullis**, C. F., and **Baddiel**, C. B. The gaseous reaction of chlorine trifluoride with methane, 5449.
**Cullis**, C. F. See also **Burgess**, A. R., 1884, 3041.
**Culvenor**, C. C. J. See **Mattocks**, A. R., 5400.
**Cummings**, W. See **Brown**, B. R., 3677.
**Cunneen**, J. I. See **Barnard**, D., 5339.
**Cureton**, P. H., **Le Fèvre**, C. G., and **Le Fèvre**, R. J. W. Molecular polarisability: the conformations of biacetyl, benzil, and furil as solutes in benzene or carbon tetrachloride, 4447.
**Currie**, A. C., **Newbold**, G. T., and **Spring**, F. S. 14-Hydroxynorcodeine and its derivatives, 4693.
**Curtis**, N. F. Trisethylenediaminenickel(II) thiosulphate as a calibrant for susceptibility measurements by the Gouy method, 3147.
**Curtis**, R. F. See **Chatterjea**, J. N., 765.

## D

**Dacre**, B., and **Wyatt**, P. A. H. The heat of autoprotolysis of sulphuric acid, 2962.
**Dale**, J. The reduction of symmetrical 1,2- and 1,3-diketones with sodium borohydride, and the separation of diastereoisomeric 1,2- and 1,3-diols by means of borate complexes, 910.
The stereochemistry of polyborate anions and of borate complexes of diols and certain polyols, 922.
**Dale**, J. See also **Hubert**, A. J., 931.
**Dalton**, F., and **Meakins**, G. D. Proof of rear approach in the oxidation of ergosterol, 1880.
**Daly**, J. J. The stereochemistry of molecules containing the C=C=N group. Part III. The crystal and molecular structure of *N*-ethyl-2,2′-dimethylsulphonylvinylideneamine, 2801.
**Daniel**, S. S., and **Salmon**, J. E. Cobalt phosphates. Part II. Phase-diagram studies of some cobalt(III) ammine phosphates, 86.
**Das Gupta**, P. C. The hemicelluloses of roselle fibre (*Hibiscus Sabdariffa*), 5262.

XUM

**Davey**, W. See **Betts**, B. E., 1683, 3333, 3340.
**David**, S. See **Birch**, A. J., 3128.
**Davidson**, G. C. See **Battersby**, A. R., 3899.
**Davidson**, T. A., and **Scott**, A. I. Oxidative pairing of phenolic radicals. Part II. The synthesis of picrolichenic acid, 4075.
**Davie**, A. W. See **Arnott**, S., 4183.
**Davies**, A. G., and **Baughan**, E. C. Antimony halides as solvents. Part II. Conductance data on solutions of organic chlorides in antimony trichloride at 75°, 1711.
**Davies**, A. G., **Hare**, D. G., and **White**, R. F. M. Peroxides of elements other than carbon. Part VII. The relative reactivity of the t-butyl and the isobutyl group in the autoxidation of di-isobutyl-t-butylboron, 341.
**Davies**, A. G., and **Packer**, J. E. Organic peroxides. Part X. The autoxidation of ethyl chaulmoograte: the course and stereochemistry of homolytic autoxidation, 4390.
**Davies**, D. See **Mandleberg**, C. J., 2031.
**Davies**, D. I., **Hey**, D. H., and **Williams**, G. H. Homolytic aromatic substitution. Part XXII. The esters formed in the reaction of benzoyl peroxide with aromatic solvents. Part XXV. The determination of the total and partial rate factors for the phenylation of naphthalene. Part XXVI. The reactions of some aroyl peroxides with naphthalene, 562, 3112, 3116.
**Davies**, J. W., and **Harris**, G. Di-*p*-(2-amino-2-carboxyethyl)-phenyl peroxide: preparation from tyrosine and probable natural occurrence in proteins, 3193.
**Davies**, M., and **Malpass**, V. E. Heats of sublimation of straight-chain monocarboxylic acids, 1048.
**Davies**, R. F. B. See **Browning**, M. C., 4816.
**Davies**, W., and **Wilmshurst**, J. R. The synthesis of polycyclic aromatic hydrocarbons. Part IV. Convenient syntheses of chrysene and three methylchrysenes, 4079.
**Davis**, B. R., **Gupta**, S. R., and **Halsall**, T. G. Studies in the synthesis of terpenes. Part VII. Synthesis of 9-methyl-6-oxo-$\Delta^{4(10)}$-1-octalylacetic acid, 4211.
**Davis**, M. See **Collins**, R. F., 1863.
**Davison**, A., **Green**, M. L. H., and **Wilkinson**, G. $\pi$-Cyclopentadienyl- and cyclopentadiene-iron carbonyl complexes, 3172.
**Davoll**, J., and **Kerridge**, K. A. The preparation of some 1- and 2-$\beta$-D-ribofuranosylpyrazolo[3,4-*d*]pyrimidines, 2589.
**Day**, A. C., **Nabney**, J., and **Scott**, A. I. Oxidative pairing of phenolic radicals. Part I. The total synthesis of griseofulvin, 4067.
**Day**, A. C. See also **Barltrop**, J. A., 3185.
**Deacon**, G. B., and **West**, B. O. Iodomercurate complexes with Group V quaternary iodides. Part I. Aqueous decompositions and absorption spectra. Part II. Reactions with triphenylphosphine, 3929, 5127.
**Dean**, B. M., **Mijović**, M. P. V., and **Walker**, J. Chemistry of micrococcin *P*. Part VI. Racemisation of 2-(1-amino-2-methylpropyl)thiazole-4-carboxylic acid, and related studies, 3394.
**Dean**, F. M., **Deorha**, D. S., **Knight**, J. C., and **Francis**, T. Spirans. Part III. The structure and stereochemistry of the ozonolysis products of 3-alkylidenegris-2′-en-4′-ones, 327.
**Dean**, F. M., and **Randell**, D. R. Derivatives of hydroxyquinol. Part III. The structure of fulvic acid: syntheses and reactions of degradation products of fulvic acid and of citromycetin, 798.
**Dean**, F. M., **Randell**, D. R., and **Winfield**, G. Derivatives of hydroxyquinol. Part II. The synthesis of 2-acetyl-4,5,7-trimethoxyindane-1,3-dione: revised structures for some degradation products from citromycetin, 792.
**Dean**, R. E., **Midgley**, A., **White**, E. N., and **McNeil**, D. The synthesis of some new phenols, 2773.
**Dean**, R. E. See also **Copeland**, P. G., 1232, 3858, 3864.
**Deane**, A. M. See **Bagnall**, K. W., 1611.
**Deavin**, A., and **Rees**, C. W. Some unusual reactions of toluene-*p*-sulphonhydrazide, 4970.
**De Belder**, A. N., **Bourne**, E. J., and **Pridham**, J. B. $\beta$-Glucopyranosides of hydroxymethyl- and hydroxyethyl-ferrocene, 4464.
**de la Mare**, P. B. D., **Klassen**, N. V., and **Koenigsberger**, R. The kinetics and mechanisms of aromatic halogen substitution. Part XI. Chlorination of phenanthrene in acetic acid, 5285.
**de la Mare**, P. B. D. See also **Beaven**, G. H., 2749.
**de Maine**, M. M. See **de Maine**, P. A. D., 1200.
**de Maine**, P. A. D., and **de Maine**, M. M. Iodine complexes in inert solvents. Part IX. The reaction between solid sodium hydroxide and iodine dissolved in inert solvents, 1200.
**Denney**, R. C. See **Ayres**, D. C., 4506.
**Denny**, P. J. See **Barrer**, R. M., 971, 983.
**Denot**, E. See **Bowers**, A., 1859.
**Deorha**, D. S. See **Dean**, F. M., 327.
**de Sousa**, J. B. See **Ho**, S. K., 1788.
**de Villiers**, J. P. The isolation and structure of gafrinin, a sesquiterpenoid lactone from *Geigeria africana*, 2049.
**Dewar**, J. H., and **Shaw**, G. Purines, pyrimidines, and glyoxalines. Part XV. Acetyluracils from amines and amino-acids. A new method for the study of *N*-terminal residues in proteins, 3254.
**Dhoubhadel**, S. P. See **Chatterjea**, J. N., 765.
**Diamantis**, A. A. See **Banks**, B. E. C., 4235.
**Dibbo**, A., **Sly**, J. C. P., **Stephenson**, L., **Walker**, T., **Warburton**, W. K., and **Whiting**, K. D. E. The synthesis of thyroxine and related compounds. Part XVII. The preparation of some additional compounds related to thyroxine, 2890.
**Dibbo**, A., **Stephenson**, L., **Walker**, T., and **Warburton**, W. K. The synthesis of thyroxine and related compounds. Part XV. The preparation of thyronines from iodonium salts and derivatives of 3,5-disubstituted tyrosines, 2645.
**Dietrich**, H., and **Hodgkin**, D. C. The crystal structure of the *trans*-dimer of nitrosoisobutane, 3686.
**Djerassi**, C., **Ollis**, W. D., and **Russell**, R. C. The relative stereochemistry of the rotenoids, 1448.
**Djerassi**, C. See aso **Bowers**, A., 1859.
**Dobinson**, B., and **Foster**, A. B. Aspects of stereochemistry. Part VI. Configuration of the 5-hydroxy-2-*p*-nitrophenyl-1,3-dioxans and further observations on *trans*-5-hydroxy-2-phenyl-1,3-dioxan, 2338.
**Dodd**, R. E., **Miller**, R. E., and **Wynne-Jones**, W. F. K. Hydrogen bonding in aqueous solutions of maleic acid, 2790.
**Doering**, W. von E., and **Helgen**, L. E. *NN′*-Di(cyclohepta-2,4,6-trienyl)urea, *alias* tropylium isocyanate, 482.
**Donaldson**, J. D., and **Moser**, W. Hydrous tin(II) oxide, 835. Basic tin(II) nitrate, 1996.
**Donaldson**, J. D., **Moser**, W., and **Simpson**, W. B. Red tin(II) oxide, 839.
**Dougill**, M. W. Phosphonitrilic derivatives. Part IX. The crystal structure of octamethylcyclotetraphosphonitrile, 5471.
**Downs**, A. J., **Ebsworth**, E. A. V., and **Emeléus**, H. J. The Raman spectra of bis(trifluoromethylthio)mercury and derived compounds, 3187.
**Doyle**, D. See **Peat**, S., 3918.
**Doyle**, F. P. See **Brain**, E. G., 633.
**Drummond**, D. W., and **Percival**, E. Structural studies on the gum exudate of *Albizzia zygia* (Macbride), 3908.
**Ducker**, J. W. See **Ansell**, M. F., 206, and **Cooley**, G., 4108.
**Duffy**, R., and **Holliday**, A. K. Trialkylplumbanes. Part I. Properties of the trimethylplumbane–borine–ammonia system, 1679.
**Duke**, A. J. See **Webb**, R. F., 4092.
**Duncan**, J. F., and **Kepert**, D. L. Polyanion equilibria in aqueous solution. Part I. The quantitative analysis of acidified tungstate solutions, 5317.
**Duncan**, J. L. See **Anderson**, D. M. W., 140, 1631, 2165, 4201, 4705.
**Duncanson**, L. A. See **Chatt**, J., 827.
**Dunn**, T. M. See **Buffagni**, S., 5105.
**Dyall**, L. K., and **Pausacker**, K. H. Free-radical substitution of pyridine 1 oxide, 18.
**Dyke**, S. F. See **Bentley**, K. W., 3151.

## E

**Eaborn**, C., **Golesworthy**, R. C., and **Lilly**, M. N. Substituent effects in fluorene compounds. Part III. Hydrolysis of 9-chloro-9-phenylfluorenes, 3052.

**Eaborn, C.,** and **Pande, K. C.** Aromatic reactivity. Part XII. Cleavage of aryltriethylgermanes by aqueous-methanolic perchloric acid. Part XVII. Cleavage of aryltricyclohexylplumbanes by aqueous-ethanolic perchloric acid. Part XXI. Effects of strongly deactivating substituents in protodetriethylgermylation, 297, 3715, 5082.

**Eaborn, C.,** and **Sperry, J. A.** Aromatic reactivity. Part XVIII. Acid cleavage of trimethylsilyl derivatives of diphenyl ether, diphenyl sulphide, furan, thiophen, benzothiophen, dibenzofuran, dibenzothiophen, and 9-ethylcarbazole, 4921.

**Eaborn, C.,** and **Taylor, R.** Aromatic reactivity. Part XIII. Effects of methyl and t-butyl groups in aromatic detritiation. Part XV. Biphenyl and naphthalene in detritiation. Part XVI. Detritiation of halogenobenzenes, 247, 1012, 2388.

**Eaborn, C.,** and **Waters, J. A.** Aromatic reactivity. Part XIV. Cleavage of aryltricyclohexyl- and aryltrimethylstannanes by aqueous-ethanolic perchloric acid, 542.

**Eaborn, C.** See also **Baker, R.**, 4927, 5077.

**Eardley, S.** See **Carrington, T. R.**, 4560.

**Earnshaw, A., Figgis, B. N., Lewis, J.,** and **Peacock, R. D.** The magnetic properties of some $d^4$-complexes, 3132.

**Earnshaw, A.,** and **Lewis, J.** Polynuclear compounds. Part I. Magnetic properties of some binuclear complexes, 396.

**Easson, A. P. T.** The search for chemotherapeutic amidines. Part XVIII. Substituted 4,4′-diamidinodiphenylamines, 1029.

**Ebsworth, E. A. V.,** and **Mays, M. J.** The preparation and properties of disilylcyanamide, 4879.

**Ebsworth, E. A. V.** See also **Downs, A. J.**, 3187.

**Eckert, J. M.,** and **Le Fèvre, R. J. W.** Molecular polarisability. Electric double refraction of solutions containing optically active solutes, 2356.

**Eckstein, Z., Gluziński, P., Hofman, W.,** and **Urbański, T.** Infrared spectra and structure of some 1,3-oxazine derivatives, 489.

**Eckstein, Z., Gluziński, P., Sobtkóa, W.,** and **Urbański, T.** Infrared absorption spectra of aliphatic nitro-alcohols. Part I. Spectra of monohydric nitro-alcohols and their chloro- and bromo-derivatives, 1370.

**Edwards, A. J.,** and **Peacock, R. D.** The structure of sodium hexafluoromolybdate(v), 4253.

**Edwards, B. F. R.** See **Cullinane, N. M.**, 3842.

**Edwards, D. A.,** and **Fowles, G. W. A.** The reaction of molybdenum(v) chloride with some aliphatic amines, 24.

**Edwards, P. N.,** and **Smith, G. F.** Akuamma alkaloids. Part II. The structure of akuammicine. Part IV. The decomposition of akuammicine in methanol, 152, 1458.

**Edwards, R. L., Lewis, D. G.,** and **Wilson, D. V.** Constituents of the higher fungi. Part I. Hispidin, a new 4-hydroxy-6-styryl-2-pyrone from *Polyporus hispidus* (Bull.) Fr., 4995.

**Edwards, R. L.,** and **Wilson, D. V.** Constituents of the higher fungi. Part II. The synthesis of hispidin, 5003.

**Edwards, T. E.** See **Peat, S.**, 29.

**Eglinton, G.** See **Bellamy, L. J.**, 4762, and **Brooks, C. J. W.**, 106, 308, 661.

**El-Abbady, A. M., Baddar, F. G.,** and **Labib, A.** β-Aroylpropionic acids. Part XIX. Further observation on the Fries rearrangement, 1083.

**El-Assal, L. S.,** and **Shehab, A. H.** β-Aroyl-α-arylmethylenepropionic acids. Part II. The synthesis and the mechanism of isomerisation of their enol lactones, 1658.

**Eley, D. D., Taylor, J. H.,** and **Wallwork, S. C.** The crystal structure of the complex $Al_2Br_6,C_6H_6$, 3867.

**El Khadem, H.** The scope and mechanism of carbohydrate osotriazole formation. Part VI. The apparent dissociation constant of triazole carboxylic acids, 3146.

**El Khadem, H., El-Shafei, Z. M.,** and **Meshreki, M. H.** The scope and mechanism of carbohydrate osotriazole formation. Part V. Chloro- and iodo-phenylosotriazoles, 2957.

**El-Kholy, I. E.-S., Rafla, F. K.,** and **Soliman, G.** Pyrone series. Part IV. 5-Aryloxy-2-pyrones. The corresponding 2-thiopyrones, pyridones, 1-hydroxy- and 1-amino-2-pyridones, and related 4,5,6-triphenyl-2-pyrones, 4490.

**Elkins, J. S.** See **Maxted, E. B.**, 5086.

**Elks, J., Oughton, J. F.,** and **Stephenson, L.** Compounds related to the steroid hormones. Part III. Phenolic ethers from the dienone–phenol rearrangement of $\Delta^{1,4}$-3-oxosteroids, 4531.

**Elks, J.,** and **Phillipps, G. H.** Compounds related to the steroid hormones. Part VII. Preparation of $\Delta^{8(11)}$-steroids from 11β-trifluoroacetates, 4573.

**Elks, J.** See aso **Bailey, E. J.**, 4535, and **Carrington, T. R.**, 4560.

**Elliott, K.,** and **Tittensor, E.** Pyranoquinolines. Part II, 2796.

**Ellis, A. J.,** and **Anderson, D. W.** The effect of pressure on the first acid dissociation constants of "sulphurous" and phosphoric acids, 1765.

The first acid dissociation constant of hydrogen sulphide at high pressures, 4678.

**Ellis, B., Hall, S. P., Petrow, V.,** and **Waddington-Feather, S.** Modified steroid hormones. Part XXIV. 16α,17α-Isopropylidenedioxy-6α-methylpregn-4-ene-3,20-dione, 4111.

**Ellis, B.** See also **Cooley, G.**, 4108.

**Elmore, D. T.** Degradative studies of peptides and proteins. Part VI. The cyclisation and degradation of *N*-phenylthiocarbamoylsarcosine derivatives, 3161.

**Elmore, N. F.,** and **King, T. J.** The synthesis of 8-isopropylpodocarpane-6,7-diol (6-hydroxytotarol) and of 7,8-dimethoxypodocarpane, 4425.

**El-Newelhy, M. F.** See **Baddar, F. G.**, 2528, 2701.

**El-Shafei, Z. M.** See **El Khadem, H.**, 2957.

**Elvidge, J. A.** Metal chelates. Part I. A micromethod for the determination of the valency of a metal in a phthalocyanine complex, 869.

**Elvidge, J. A.,** and **Jackman, L. M.** Studies of aromaticity by nuclear magnetic resonance spectroscopy. Part I. 2-Pyridones and related systems, 859.

**Elvidge, J. A.,** and **Lever, A. B. P.** Metal chelates. Part II. Phthalocyanine–chromium complexes and perpendicular conjugation, 1257.

**Elworthy, P. H.** The adsorption of water vapour by lecithin and lysolecithin, and the hydration of lysolecithin micelles, 5385.

**El-Zimaity, M. T.** See **Baddar, F. G.**, 2701.

**Emeléus, H. J.,** and **MacDuffie, D. E.** Preparation and properties of trifluoromethylthiosilver, 2597.

**Emeléus, H. J.,** and **Mackay, K. M.** Conductimetric titration of sodium in liquid ammonia with phosphine, arsine, stibine, and germanes, 2676.

**Emeléus, H. J.** See also **Downs, A. J.**, 3187.

**England, B. D.** See **Alet, I. R.**, 5259.

**Essery, J. M.,** and **Schofield, K.** The influence of steric factors on the properties of 4-aminopyridine derivatives, 3939.

**Evans, A. G.,** and **George, D. B.** The catalytic action of anionic catalysts. Part I. The interaction of butyllithium with 1,1-diphenylethylene, 4653.

**Evans, A. G., James, E. A.,** and **Owen, E. D.** The activation of carbon–carbon double bonds by cationic catalysts. Part X. The reaction between 1,1,3,3-tetraphenylbut-1-ene, antimony trichloride, and hydrogen chloride in benzene, 3532.

**Evans, A. G.,** and **Owen G. D. T.** The catalytic action of metal alkyl–metal halide in complexes. Part I. The dimerisation of 1,1-diphenylethylene in benzene–n-butyllithium–titanium tetrachloride–hydrogen chloride systems, 1733.

**Evans, D. F.** Magnetic perturbation of singlet–triplet transitions. Part V. Mechanism. Part VI. Octa-1,3,5,7-tetraene, 1987, 2566.

**Evans, R. F.,** and **Kynaston, W.** Studies of the coal-tar bases. Part IX. A new method of isolation of 2,3-dimethyl- and 2,4,6-trimethyl-pyridine, 5556.

## F

**Falconer, W. E., Hunter, T. F.,** and **Trotman-Dickenson, A. F.** The thermal isomerization of cyclopropane, 609.

**Falconer, W. E., Knox, J. H.,** and **Trotman-Dickenson, A. F.** Competitive oxidations. Part II. The lower alkanes and cyclopropane. Part III. Oxidations at low temperatures induced by light, 782, 4285.

**Fanshawe, R. S.** See **Aspinall, G. O.**, 4215.

**Farhat-Aziz,** and **Moelwyn-Hughes, E. A.** The kinetics of the reaction between methyl fluoride and lithium iodide in acetone solution, 1523.

XUM

**Faulkner**, J. K., and **Woodcock**, D. Fungal detoxication. Part V. Metabolism of *o*- and *p*-chlorophenoxyacetic acids by *Aspergillus niger*, 5397.

**Feakins**, D. Washburn numbers in the methanol–water–hydrochloric acid system at 25°.

**Feeney**, J., **Holliday**, A. K., and **Marsden**, F. J. Diboron tetrachloride–olefin compounds. Part III. The reaction of diboron tetrachloride with trichloroethylene, isobutene, and *cis*- and *trans*-but-2-ene, 356.

**Ferguson**, G., **Fritchie**, C. J., **Robertson**, J. M., and **Sim**, G. A. The crystal and molecular structure of (+)-10-bromo-2-chloro-2-nitrosocamphane, 1976.

**Ferrier**, R. J. The interaction of phenylboronic acid with hexosides, 2325.

**Ferris**, R. T., and **Hamer**, D. Isobutyl and t-butyl derivatives of 2-methoxynaphthalene, 1409.

**Fettis**, G. C., and **Trotman-Dickenson**, A. F. The reactions of methyl and ethyl radicals with hydrogen bromide and the strength of C–H bonds, 3037.

**Ficken**, G. E., and **Kendall**, J. D. Diazaindenes and their quaternary salts. Part II. The cyclisation of isopropyl methyl ketone 3-pyridylhydrazone, 584.
2,3-Dihydro-3,3-dimethyl-1*H*-1,7-diazaindan-2-one, 747.

**Fielding**, B. C., **Holker**, J. S. E., **Jones**, D. F., **Powell**, A. D. G., **Richmond**, K. W., **Robertson**, A., and **Whalley**, W. B. The chemistry of fungi. Part XXXIX. The structure of monascin, 4579.

**Figgis**, B. N., **Lewis**, J., and **Mabbs**, F. E. The magnetic properties of some $d^3$-complexes, 3138.

**Figgis**, B. N. See also **Earnshaw**, A., 3132.

**Finar**, I. L. The structure of 1,5-diketones, 674.

**Finar**, I. L., and **Manning**, M. The preparation and some reactions of 4-formyl-1-phenylpyrazoles, 2733.

**Finar**, I. L., and **Miller**, D. B. The orientation of some bromo-1-phenylpyrazoles, 2769.

**Finar**, I. L., and **Montgomery**, A. J. The preparation and oxidation of sulphides formed from *o*-nitrobenzenesulphenyl chloride and ketones, 367.

**Firth**, J. G. See **Tyrrell**, H. J. V., 3432.

**Fischer**, A., **Mann**, B. R., and **Vaughan**, J. Influence of pressure on the Hammett reaction constant: dissociation of benzoic acids and phenylacetic acids, 1093.

**Fischer**, E. See **Heiligman-Rim**, R., 156.

**Fischer**, E. O. See **Fritz**, H. P., 547.

**Fleming**, I., and **Harley-Mason**, J. Geometrical isomerism in an azine, 5560.

**Fleming**, I. D. See **Archibald**, A. R., 1183.

**Fleming**, R. The activity coefficients of aqueous solutions of choline chloride at 25°, 3100.

**Fletcher**, J. M., **Greenfield**, B. F., **Hardy**, C. J., **Scargill**, D., and **Woodhead**, J. L. Ruthenium red, 2000.

**Fletcher**, J. M., **Scargill**, D., and **Woodhead**, J. L. The nitrous acid–tributyl phosphate complex, 1705.

**Fletcher**, J. M. See also **Woodhead**, J. L., 5039.

**Fletcher**, T. L., and **Namkung**, M. J. Derivatives of fluorene. Part XII. 2-Amino-9-bromofluorene hydrobromide and related compounds, 1400.

**Flowers**, M. C., and **Frey**, H. M. The thermal unimolecular isomerisation of vinylcyclopropane to cyclopentene, 3547.
The thermal isomerization of spirobicyclopropane, 5550.

**Fodor**, G., and **Csepreghy**, G. The stereochemistry of the tropane alkaloids. Part XIV. The absolute configuration of (−)-tropic acid, hyoscyamine, and hyoscine, 3222.

**Fodor**, G., **Vincze**, I. W., and **Tóth**, J. The stereochemistry of the tropane alkaloids. Part XIII. The absolute configuration and a simplified syntheses of valeroidine, 3219.

**Forbes**, M. H., **Heineky**, D. M., **Mann**, F. G., and **Millar**, I. T. Cyclic diarsines. Part VI. The thermal decomposition of some cyclic quaternary diarsonium dihydroxides and dibromides, 2762.

**Ford-Smith**, M. H. See **Bell**, R. P., 1413.

**Forrest**, H. S., **Hatfield**, D., and **Lagowski**, J. M. Uric acid riboside. Part I. Isolation and reinvestigation of the structure, 963.

**Foster**, A. B., **Haines**, A. H., **Homer**, J., **Lehmann**, J., and **Thomas**, L. F. Aspects of stereochemistry. Part VIII. Determination of the configuration at the benzylidene acetal carbon atoms in 4,6-*O*-benzylidene-D-glucose and 1,3-*O*-benzylidene-L-arabinitol by nuclear magnetic resonance spectroscopy, 5005.

**Foster**, A. B., **Haines**, A. H., and **Lehmann**, J. Aspects of stereochemistry. Part IX. Structure of the di-*O*-benzylidenetetritols, 5011.

**Foster**, A. B., **Lehmann**, J., and **Stacey**, M. Ionophoresis of carbohydrates. Part VII. 2,5-Di-*O*-methyl-L-rhamnose: its ionophoresis and conversion into 6-deoxy-2,5-di-*O*-methyl-L-altrose, 4649.

**Foster**, A. B., **Martlew**, E. F., **Stacey**, M., **Taylor**, P. J. M., and **Webber**, J. M. Amino-sugars and related compounds. Part VIII. Some properties of 2-deoxy-2-sulphoamino-D-glucose, heparin, and related substances, 1204.

**Foster**, A. B., **Olavesen**, A. H., and **Webber**, J. M. Reaction of L-threitol with acetone, 5095.

**Foster**, A. B. See also **Bolton**, C. H., 4831, **Buck**, K. W., 3633, and **Dobinson**, B., 2338.

**Foster**, A. G., and **Siddiqi**, I. R. Activity coefficients of non-electrolytes in aqueous solutions of sugars, 4906.

**Foster**, R. See **Champion**, N. G. S., 5060.

**Foster**, W. R. See **Cadogan**, J. I. G., 3071, 3076.

**Fowell**, P. A., and **Mortimer**, C. T. Heats of formation and bond energies. Part V. n-Butyl-lithium, 3793.

**Fowles**, G. W. A., and **Nicholls**, D. The ammonolysis of hexahalogenotitanates, 95.

**Fowles**, G. W. A. See also **Edwards**, D. A., 24.

**Francis**, K. E. See **Mandleberg**, C. J., 2464.

**Francis**, R., and **Cotton**, F. A. Complexes of tetrahydrothiophen oxide, 2078.

**Francis**, T. See **Dean**, F. M., 327.

**Frankel**, M., and **Gertner**, D. Syntheses of some polymeric polypeptides of lanthionine, 459.
Syntheses of poly-(*S*-alkyl-DL-homocysteines), poly-DL-homocysteine, and poly-DL-homocysteic acid, 463.

**Frazer**, M. J. Interaction between selenium oxychloride and the trichlorides of boron and aluminium, 3165.

**Frazer**, M. J., **Gerrard**, W., and **Singh**, A. P. Interaction of trialkyl phosphates with silicon chlorides, 4680.

**Frazer**, M. J. See also **Cooper**, S., 5545.

**Fredericks**, P. S., and **Tedder**, J. M. Free-radical substitution in aliphatic compounds. Part III. Halogenation of the 2-halogenobutanes, 3520.

**French**, C. M., and **Monks**, E. R. The conductance of ferric and cupric stearates in aliphatic hydrocarbons, 466.

**French**, C. M., and **Tomlinson**, R. C. B. The conductance of solutions in which the solvent molecule is "large." Part VII. Solutions in triaryl phosphites, 311.

**French**, P. V., **Roubinek**, L., and **Wassermann**, A. Preparation and properties of deeply coloured, electrically conducting polymers, 1953.

**Frey**, H. M. See **Flowers**, M. C., 3547, 5550.

**Fritchie**, C. J. See **Ferguson**, G., 1976.

**Fritz**, H. P., and **Fischer**, E. O. Dicyclopentadienyl-tin and -lead, 547.

**Fuller**, G., and **Tatlow**, J. C. Some isomeric hexafluorocyclobutanes and pentafluorocyclobutenes, 3198.

## G

**Gaaf**, J. See **Aalbersberg**, W. Ij., 905.

**Gaimster**, K. See **Bretherick**, L., 2919.

**Ganguly**, A. K., and **Seshadri**, T. R. Leucoanthocyanidins of plants. Part III. Leucopelargonidin from *Eucalyptus calophylla* Kino, 2787.

**Ganguly**, A. K. See also **Autrey**, R. L., 3313.

**Garbutt**, S. See **Anderson**, D. M. W., 5230.

**Garcia**, L., and **Orchin**, M. Ethylene-platinous chloride pyridine *N*-oxide, 2254.

**Gardner**, J. N., **Lowe**, G., and **Read**, G. Chemistry of the higher fungi. Part XII. The enzymic decarboxylation of an αβ-acetylenic acid, 1532.

**Garraway**, J. L. The preparation of some 3-substituted rhodanines and their thiazine analogues, 3733.

**Gawat**, M. See **Balaban**, A. T., 3564.

**Gee**, G., **Higginson**, W. C. E., **Taylor**, K. J., and **Trenholme**, M. W. The polymerization of epoxides. Part III. The polymerization of propylene oxide by sodium alkoxides, 4298.

**George**, D. B. See **Evans**, A. G., 4653.
**Gero**, S. D. See **Angyal**, S. J., 4116.
**Gerrard**, W., and **Griffey**, P. F. Interaction of trialkyl phosphates with boron trichloride, 4095.
**Gerrard**, W., **Mooney**, E. F., and **Willis**, H. A. Substitution patterns of monosubstituted benzene derivatives, 3153.
Structure of phosphoryl chloride–boron trichloride complex, 4255.
**Gerrard**, W. See also **Cooper**, S., 5545, and **Frazer**, M. J., 4680.
**Gertner**, D. See **Frankel**, M., 459, 463.
**Gething**, B., **Patrick**, C. R., and **Tatlow**, J. C. Aromatic polyfluoro-compounds. Part IX. Perfluoro-*o*-xylene, perfluoro-*p*-xylene, and tetrafluoro-phthalic and -terephthalic acid, 1574.
**Ghaly**, E. H. See **Baddar**, F. G., 2528.
**Gibson**, M. S. 10-Methylphenanthridine, 2249.
Applications of the "abnormal" Reimer–Tiemann reaction, 2251.
**Giles**, C. H., **Greczek**, J. J., and **Nakhwa**, S. N. Studies in adsorption. Part XIII. Anomalous (endothermic) effects of adsorption on inorganic solids, 93.
**Giles**, C. H., and **McKay**, R. B. Studies in adsorption. Part XII. Mechanism of adsorption of aromatic hydrocarbons by chromatographic alumina, 58.
**Giles**, C. H., **McKay**, R. B., and **Good**, W. Studies in hydrogen-bond formation. Part X. Complex-formation between a variety of organic solutes in carbon tetrachloride, 5434.
**Giles**, C. H., **Rahman**, S. M. K., and **Smith**, D. Studies in the light absorption of dyes. Part III. Absorption spectra of dyes in solution and adsorbed in solid films, 1209.
**Gill**, N. S. Complex halides of the transition metals. Part II. Tetrahedral iron complexes, 3512.
**Gillard**, R. D. See **Irving**, H., 2249.
**Gillespie**, R. J. See **Blakely**, C. F., 1939.
**Gilson**, T. See **Beattie**, I. R., 2585.
**Ginsberg**, A. E. See **Banks**, R. E., 1740.
**Ginsberg**, D. See **Altman**, Y., 1498, and **Strumza**, J., 1505, 1512, 1514.
**Glen**, N. A. See **Carruthers**, W., 5251.
**Glockling**, F., **Hooton**, K., and **Kingston**, D. Mesityl and phenyl derivatives of lead, 4405.
**Gluziński**, P. See **Eckstein**, Z., 489, 1370.
**Godfrey**, L. E. A., and **Kurzer**, F. Heterocyclic compounds from urea derivatives. Part II. Synthesis and cyclisation of 4-substituted 1-amidino-semicarbazides and -thiosemicarbazides, 5137.
**Godin**, P. J. See **Büchi**, G., 2843, and **Crombie**, L., 2861, 2876.
**Gold**, V., and **Riley**, T. Kinetic measurements of the acetylation of anisole by acetic acid in the presence of boron trifluoride, 1676.
**Gold**, V. See also **Butler**, A. R., 2305, 4362.
**Golden**, J. H. Poly-*p*-xylylene and related polymers, 1604.
Bi(anthracene-9,10-dimethylene) (tetrabenzo-[2,2]-paracyclophane), 3741.
**Goldwhite**, H., **Hasseldine**, R. N., and **Mukherjee**, R. N. Polyfluoroalkylmercuric fluorides, 3825.
**Golesworthy**, R. C. See **Eaborn**, C., 3052.
**Good**, W. See **Giles**, C. H., 5434.
**Goodgame**, D. M. L., and **Cotton**, F. A. Phosphine oxide complexes. Part IV. Tetrahedral, planar, and binuclear complexes of copper(II) with phosphine oxides, and some arsine oxide analogues. Part V. Tetrahedral complexes of manganese(II) containing triphenylphosphine oxide, and triphenylarsine oxide as ligands, 2298, 3735.
**Goodrich**, B. S. See **Shoppee**, C. W., 1583.
**Goosen**, A., **John**, E. V. O., **Warren**, F. L., and **Yates**, K. C. The alkaloids of the amaryllidaceae. Part IX. Racemisation of buphanitine (Nerbowdine) during Oppenauer oxidations, 4038.
**Gorrie**, J. R. See **Bell**, F., 4258.
**Gough**, S. T. D., and **Trippett**, S. The reduction of alkyltriphenylphosphonium halides with lithium aluminium hydride, 4263.
**Grace**, J., and **Symons**, M. C. R. A kinetic study of the hydrolysis of certain alkyl acetates and corresponding lactones, 47.
**Graham**, W. See **Attenburrow**, J., 4547.
**Graham-Bryce**, I. J. See **Corkill**, J. M., 3893.
**Gramshaw**, J. W. See **Armitage**, R., 1842.
**Grant**, P. K. See **Carman**, R. M., 2187.
**Gray**, C. H., **Kulczycka**, A., and **Nicholson**, D. C. The chemistry of the bile pigments. Part III. Prototropy of bilirubin to a verdinoid pigment. Part IV. Spectrophotometric titration of the bile pigments, 2268, 2276.
**Gray**, C. H., **Kulczycka**, A., **Nicholson**, D. C., and **Petryka**, Z. The chemistry of the bile pigments. Part II. The preparation and spectral properties of biliverdin, 2264.
**Gray**, G. W., and **Lewis**, D. Some new di- and tri-nitro-*p*-terphenyls, 1069.
Isomer ratios for the mononitration of *p*-terphenyl in acetic acid and acetic anhydride, 5156.
**Gray**, H. B. See **Basolo**, F., 2207.
**Gray**, P., **Pearson**, M. J., and **Rathbone**, P. 1-Phenylethoxyl radicals in the thermal decomposition of 1-phenylethyl nitrite, 4006.
**Gray**, P., **Rathbone**, P., and **Williams**, A. Alicyclic alkoxyl radicals in the thermal decompositions of cyclohexyl and 1-methylcyclohexyl nitrite, 2620.
**Grdenić**, D. See **Kamenar**, B., 3954.
**Greczek**, J. J. See **Giles**, C. H., 93.
**Green**, B. See **Apsimon**, J. W., 752.
**Green**, G. F. H., and **Long**, A. G. Compounds related to the steroid hormones. Part II. The action of hydrogen bromide on 2-bromo-3-oxo-$\Delta^1$-5α-steroids, 2532.
**Green**, G. F. H. See also **Carrington**, T. R., 4560.
**Green**, J. H. S. The thermodynamic properties of organic oxygen compounds. Part II. Vibrational assignment and calculated thermodynamic properties of phenol. Part III. Formic acid, 2236, 2241.
**Green**, M. L. H., **McCleverty**, J. A., **Pratt**, L., and **Wilkinson**, G. The di-π-cyclopentadienyl hydrides of tantalum, molybdenum, and tungsten, 4854.
**Green**, M. L. H. See also **Davison**, A., 3172.
**Greenfield**, B. F. See **Fletcher**, J. M., 2000, and **Hardy**, C. J., 90, 174.
**Greenock**, I. A. See **Battersby**, A. R., 2592.
**Greenwood**, C. T., and **Thomson**, J. Physicochemical studies on starches. Part XXIII. Some physical properties o Floridean starch and the characterization of structure-type of branched α-1,4-glucans, 1534.
**Greenwood**, C. T. See also **Aspinall**, G. O., 3667.
**Greenwood**, N. N., and **Osborn**, A. J. Chemical and magnetic properties of lanthanum dicarbide and sesquicarbide, 1775.
**Gregg**, S. J., and **Jepson**, W. B. The oxidation of calcium in moist oxygen, 884.
**Gregg**, S. J., and **Pope**, M. I. The production of active solids by thermal decomposition. Part XIII. The calcination of ion-free hydrous titania, 1252.
**Gregory**, G. I., and **Long**, A. G. The Mannich reaction with cholesta-1,4-dien-3-one, 3059.
**Gregory**, G. I. See also **Carrington**, T. R., 4560.
**Gregory**, H. See **Bu'Lock**, J. D., 3544.
**Greig**, C. G., **Leaback**, D. H., and **Walker**, P. G. The preparation of phenyl 2-amino-2-deoxy-β-D-glucopyranoside and some 2-acylamino-derivatives thereof, 879.
**Griffey**, P. F. See **Gerrard**, W., 4095.
**Griffith**, W. P., **Lewis**, J., and **Wilkinson**, G. Studies on transition-metal–nitric oxide complexes. Part VI. Platinum, palladium, and nickel complexes, 775.
Bis(triphenylphosphine)nickel dinitrosyl, 2259.
**Grimshaw**, J. See **Birch**, A. J., 1407, 2286, 5194.
**Grove**, J. F. Gibberellin $A_2$, 3545.
**Grove**, J. F., and **Riley**, B. J. Studies in the preparation of B-nor-diterpenoids, 1105.
**Grove**, J. F. See also **Cross**, B. E., 2498.
**Grzybowska**, B., **Knox**, J. H., and **Trotman-Dickenson**, A. F. The reaction of methylene with buta-1,3-diene, 4402.
**Gunstone**, F. D. See **Carruthers**, W., 5251.
**Gupta**, S. R., **Halsall**, T. G., and **Jones**, E. R. H. The chemistry of triterpenes and related compounds. Part XLI. The bromination of lupeol and its esters, 5353.
**Gupta**, S. R. See also **Davis**, B. R., 4211.
**Guthrie**, R. D. Periodate oxidation. Part VI. Infrared spectra of some hemialdal esters, 2525.

**Guthrie**, R. D., and **Johnson**, L. F. Nitrogen-containing carbohydrate derivatives. Part I. Methyl 4,6-*O*-benzylidene-3-deoxy-3-phenylazo-α-D-glucoside, 4166.
**Gutt**, W. See **Welch**, J. H., 4442.
**Guy**, R. G. See **Adams**, D. M., 738, **Bacon**, R. G. R., 2428, 2436, and **Chatt**, J., 827, 2332.

H

**Hacket**, N., and **Le Fèvre**, R. J. W. Molecular polarisability. The anisotropies of the molecules $PCl_3$, $OPCl_3$, $NMe_3$, and $ONMe_3$, 2612.
**Haddad**, Y. M. Y. See **Bancroft**, G., 3295, and **Sondheimer**, F., 767.
**Hadwick**, T. See **Bunton**, C. A., 943.
**Haines**, A. H. See **Foster**, A. B., 5005, 5011.
**Hall**, A. N., **Hollingshead**, S., and **Rydon**, H. N. The acid and alkaline hydrolysis of some substituted phenyl α-D-glucosides, 4290.
**Hall**, L. D., **Hough**, L., and **Pritchard**, R. A. The epoxide–episulphide transformation, 1537.
**Hall**, S. P. See **Ellis**, B., 4111.
**Hallas**, G. See **Barker**, C. C., 1285, 1395, 1529, 2342.
**Halliwell**, A. See **Arcus**, C. L., 3708.
**Halmann**, M., **Kugel**, L., and **Pinchas**, S. The structure of "Boyd's chloride" (triphenylmethylphosphonic dichloride), 3542.
**Halmann**, M., **Lapidot**, A., and **Samuel**, D. Hydrolysis of *N*-acylphosphoramidic acids. Part IV. *N*-Benzenesulphonylphosphoramidic acid, 3158.
**Halsall**, T. G., and **Hanes**, A. R. Studies in the synthesis of terpenes. Part VI. Some reactions of 3-methylbutane-1,3-diol, 3251.
**Halsall**, T. G. See also **Akisanya**, A., 3705, **Baddeley**, G. V., 3891, **Brewis**, S., 646, **Chaudhry**, G. R., 2725, **Davis**, B. R., 4211, and **Gupta**, S. R., 5353.
**Hambling**, J. K., **Hey**, D. H., **Orman**, S., and **Williams**, G. H. Homolytic aromatic substitution. Part XXIV. The *p*-methylphenylation of nitrobenzene and chlorobenzene, 3108.
**Hamer**, D., and **Leckey**, R. G. Carboxymethyldichloroarsine and related carboxylic acids containing arsenic, 1398.
**Hamer**, D. See also **Ferris**, R. T., 1409.
**Hamied**, Y. K. See **Cromartie**, R. I. T., 3622.
**Hammick**, D. L., and **Voaden**, D. J. Chemical and physical properties of some sydnones, 3303.
**Hands**, A. R. See **Acheson**, R. M., 744, 746, and **Halsall**, T. G., 3251.
**Hanna**, S. B., **Iskander**, Y., and **Riad**, Y. The influence of the nitro-group upon side-chain reactivity. Part I. The reaction between 4-nitrobenzyl chloride and alkali, 217.
**Hanna**, S. B., **Iskander**, Y., and **Salama**, A. The influence of the nitro-group upon side-chain reactivity. Part II. The inhibition of the influence of the nitro-group upon α-proton-extraction from 4-nitrobenzyl chloride, 221.
**Harada**, Y. See **Birch**, A. J., 889.
**Hardisson**, A. See **Barber**, M. S., 1625.
**Hardy**, C. J., **Greenfield**, B. F., and **Scargill**, D. The extraction of nitric acid from aqueous solution by organic solvents: the dimerisation of nitric acid in the organic solvent, 90.
The solvent-extraction of beryllium from aqueous solutions of mineral acids by alkyl esters of phosphoric acid, 174.
**Hardy**, C. J., and **Scargill**, D. The dissolution of beryllium in aqueous solutions of mineral acids and ammonium fluoride, 2658.
**Hardy**, C. J. See also **Fletcher**, J. M., 2000.
**Hardy**, F. E. See **Baddiley**, J., 2180.
**Hare**, D. G. See **Davies**, A. G., 341.
**Hargitay**, B. See **Hubert**, A. J., 931.
**Hargreaves**, G. B. See **Cady**, G. H., 1563, 1568.
**Harle**, A. J. See **Casimir**, D. J., 5297.
**Harley-Mason**, J. See **Bick**, I. R. C., 1896, and **Fleming**, I., 5560.
**Harnden**, M. R. See **Barker**, S. A., 5256.
**Harper**, J. S. See **Brown**, D. J., 1298.
**Harrap**, K. R. See **Bergel**, F., 4051.
**Harris**, A. P., and **Weale**, K. E. Liquid-phase reactions at high pressures. Part XIII. Structural effects in the acceleration of Menschutkin reactions by pressure, 146.
**Harris**, G., and **MacWilliam**, I. C. Syntheses of peptidyl-nucleotidates including L-arginyl-L-alanyl-L-arginyl-L-alanyl uridine-5′ phosphate, 2053.
**Harris**, G. See also **Davies**, J. W., 3193.
**Harris**, R. K., and **Packer**, K. J. High-resolution nuclear magnetic resonance spectra of pentafluorosulphur compounds, 4736.
**Harrison**, D., and **Smith**, A. C. B. Acyl derivatives of 2-oxobenzimidazoline, 4827.
**Harrow**, G. A. See **Spice**, J. E., 3021.
**Hart**, F. A. See **Chatt**, J., 1416, 5504.
**Hart**, G., **Liljegren**, D. R., and **Potts**, K. T. 3-Acetylindole, 4267.
**Hartigan**, J. See **Bourne**, E. J., 1088.
**Hartley**, S. B., **Paddock**, N. L., and **Searle**, H. T. Phosphonitrilic derivatives. Part IV. The heats of formation of the trimeric and tetrameric phosphonitrilic chlorides, 430.
**Harvey**, D. R., and **Norman**, R. O. C. The *ortho* : *para*-ratio in aromatic substitution. Part II. Chlorination with t-butyl hypochlorite, 3604.
**Harvey**, W. E. See **Andrews**, E. D., 4687.
**Haslam**, E., **Haworth**, R. D., **Jones**, K., and **Rogers**, H. J. Gallotannins. Part I. Introduction: and the fractionation of tannase, 1829.
**Haslam**, E., **Haworth**, R. D., and **Knowles**, P. F. Gallotannins. Part IV. The biosynthesis of gallic acid, 1854.
**Haslam**, E., **Haworth**, R. D., **Mills**, S. D., **Rogers**, H. J., **Armitage**, R., and **Searle**, T. Gallotannins. Part II. Some esters and depsides of gallic acid, 1836.
**Haslam**, E., **Haworth**, R. D., and **Makinson**, G. K. Synthesis of 3-*O*-*p*-coumaroylquinic acid, 5153.
**Haslam**, E. See also **Armitage**, R., 1842.
**Hassall**, C. H., and **Lewis**, J. R. The biosynthesis of phenols. Part III. Oxidative coupling leading to geodoxin and related compounds, 2312.
**Hassan**, M. See **Beaven**, G. H., 2749.
**Hasszeldine**, R. N., and **Nyman**, F. Reactions of fluorocarbon radicals. Part XVI. Photolysis of some perhalogenoacetones, 3015.
**Hasszeldine**, R. N. See also **Banks**, R. E., 1740, **Barr**, D. A., 1351, **Birchall**, J. M., 2204, 3719, and **Goldwhite**, H., 3825.
**Hatfield**, D. See **Forrest**, H. S., 963.
**Hathaway**, B. J., **Holah**, D. G., and **Postlethwaite**, J. D. The preparation and properties of some tetrakis(methyl cyanide)-copper(I) complexes, 3215.
**Hathaway**, B. J., and **Underhill**, A. E. The infrared spectra of some transition-metal perchlorates, 3091.
**Hawkins**, E. G. E., and **Thompson**, R. D. 2-Phenylbutadiene from α-methylstyrene, 370.
**Haworth**, R. D. See **Armitage**, R., 1842, and **Haslam**, E., 1829, 1836, 1854, 5153.
**Haws**, E. J., and **Holker**, J. S. E. The chemistry of fungi. Part XXXVIII. Further evidence for the structure of rubropunctatin, 3820.
**Hay**, M. See **Bu'Lock**, J. D., 3544.
**Hayon**, E., and **Weiss**, J. J. The chemical action of ionising radiations on simple aliphatic alcohols. Part I. Irradiation of ethanol in the liquid and in the solid state and in the presence of solutes. Part II. Irradiation of methanol in the absence and in the presence of oxygen in the solid and in the liquid state, 3962, 3970.
**Hayter**, R. G. See **Chatt**, J., 772, 896, 2605, 5507.
**Head**, F. S. H., and **Williamson**, M. M. Mixed formals derived from alcohols and phenols, 2578.
**Heath**, D. F., and **Mattocks**, A. R. Preparation of $^{14}C$-labelled dialkylnitrosamines, and an improved preparation of *N*-methyl-*N*-t-butylamine, 4226.
**Heaton**, B. G. See **Baddeley**, G., 3828, 3835, 4306.
**Heertjes**, P. M., and **Beek**, H. C. A. van. Derivatives of benzo-1,4-dioxan. Part V, 2148.
**Heffernan**, M. L., and **White**, R. F. M. The nuclear magnetic resonance spectra of triphosphonitrilic, 1,1-difluoride 3,3,5,5-tetrachloride, 1382.
**Heffernan**, M. L. See also **Craig**, D. P., 1376.

**Heilignan-Rim, R., Hirshberg, Y., and Fischer, E.** Photochromism in some spiropyrans. Part III. The extent of phototransformation, 156.
**Heinekey, D. M.** See **Forbes, M. H.**, 2762.
**Heigen, L. E.** See **Doering, W. von E.**, 482.
**Helmy, A. A. A.** See **Tadros, W.**, 2687.
**Henbest, H. B., Jones, D. N., and Slater, G. P.** Reactions of ketones with oxidising agents. Part I. Catalysis of the ketone–lead tetra-acetate reaction with boron trifluoride, 4472.
**Henbest, H. B., and McEntee, J.** Aspects of stereochemistry. Part XVIII. Synthesis of the 10-methyldecalin-2,9-diols, 4478.
**Henbest, H. B., Reid, J. A. W., and Stirling, C. J. M.** The oxidation of ethers and related compounds. Part I. The thermal and photochemical decomposition of t-butyl peroxide in anisole, 5239.
**Hey, D. H., Leonard, J. A., Moynehan, T. M., and Rees, C. W.** Internuclear cyclisation. Part XVI. Abnormal reactions of diazonium salts from *N*-alkyl-2-amino-2′- and -4′-methoxybenzanilides. A new dienone–phenol rearrangement, 232.
**Hey, D. H., Orman, S., and Williams, G. H.** Homolytic aromatic substitution. Part XXIII. A redetermination of the relative rate of phenylation of nitrobenzene, 565.
**Hey, D. H., Perkins, M. J., and Williams, G. H.** 2,4′-Diphenylbiphenyl [*op*′-quaterphenyl], 748.
**Hey, D. H., Saunders, F. C., and Williams, G. H.** Homolytic aromatic substitution. Part XXI. The arylation of benzotrihalides, 554.
**Hey, D. H.** See also **Ahmad, Y.**, 3882, **Brown, D. N.**, 3873, **Cadogan, J. I. G.**, 3879, 5236, **Davies, D. I.**, 562, 3112, 3116, and **Hambling, J. K.**, 3108.
**Hichens, M.** See **Acheson, R. M.**, 650.
**Hichens, R. E.** See **Acheson, R. M.**, 650.
**Hickinbottom, W. J.** See **Barnes, T. J.**, 953, 2616, **Blackwell, J.**, 1405, and **Booccock, J. R. B.**, 2587.
**Hickling, A., and Newns, G. R.** Glow-discharge electrolysis. Part IV. The formation of hydrazine in liquid ammonia. Part V. The contact glow-discharge electrolysis of liquid ammonia, 5177, 5186.
**Higginson, W. C. E.** See **Gee, G.**, 4298.
**Hill, J. A., Johnson, A. W., and King, T. J.** The synthesis of podocarpane-6,7-diol, a degradation product of maytenone, 4430.
**Hilpern, J. W.** See **Baker, W.**, 479.
**Hinton, I. G., and Webb, R. F.** The disproportionation of carbodi-imides, 5051.
**Hinton, R. C., Mann, F. G., and Todd, D.** The abnormal hydrolysis of certain β-(diarylphosphino)propionic esters. Part I, 5454.
**Hirshberg, Y.** See **Heiligman-Rim, R.**, 156.
**Ho, S. K., and De Sousa, J. B.** Alkoxy-radicals. Part I. The kinetics of thermal decomposition of dibenzyl hyponitrite in solution, 1788.
**Hoare, J. L.** See **Briggs, L. H.**, 4645.
**Hodge, N.** See **Addison, C. C.**, 2490, 2987.
**Hodges, R.** Constituents of the leaves of *Thujopsis dolabrata*, 4247.
**Hodgkin, D. C.** See **Dietrich, H.**, 3686.
**Hoehn, H. H., Pratt, L., Watterson, K. F., and Wilkinson, G.** Transition-metal fluorocarbon complexes. Part I. Derivatives of perfluoro-olefins, 2738.
**Hoffman, E.** See **Bergmann, E. D.**, 3452.
**Hofman, W.** See **Eckstein, Z.**, 489.
**Hogg, W., McKinnon, D. M., Trotman-Dickenson, A. F., and Verbeke, G. J. O.** The pyrolysis of 1,3,5-trioxan, 1403.
**Holah, D. G.** See **Hathaway, B. J.**, 3215.
**Holan, G., and Samuel, E.** The synthesis of 3-alkyl-1-arylsulphonyl-hydantoins and -2-thiohydantoins, 4660.
**Holker, J. S. E.** See **Fielding, B. C.**, 4579, and **Haws, E. J.**, 3820.
**Holliday, A. K., Marsden, F. J., and Massey, A. G.** The reactions of diboron tetrachloride with some nitrogen-containing donor molecules, 3348.
**Holliday, A. K.** See also **Duffy, R.**, 1679, **Feeney, J.**, 356, and **Massey, A. G.**, 1893.
**Hollingshead, S.** See **Hall, A. N.**, 4290.
**Hollingsworth, B. L., and Petrow, V.** Some αω-di(phenanthridin-6-yl)alkanes, 3664.
Some derivatives of biphenyl and of phenanthridine, 3771.
**Hollingsworth, B. L.** See also **Brown, R. J.**, 4295.
**Holmes, F., Jones, K. M., and Torrible, E. G.** Complex-forming agents similar to 2,2′-bipyridyl. Part I. Some ligands containing imidazole, 4790.
**Holmes, W. S.** See **Chapman, A. C.**, 1825.
**Holt, G., and Pagdin, B.** The action of aluminium chloride on some *o*-alkylbenzenesulphonic acids and *o*-alkyldiphenyl sulphones, 4514.
**Holt, P. F., Hopson-Hill, B. I., and McNae, C. J.** Polycyclic cinnoline derivatives. Part VII. Benzo[*c*][$^{15}$N]cinnoline, 1404.
**Holt, P. F., and McNae, C. J.** The diazo-exchange reaction studied with nitrogen-15 : *p*-nitrophenyldiazonium chloride solution, 1825.
**Holt, P. F.** See also **Corbett, J. F.**, 1363, 3695, 4261, 5029.
**Holton, P. G.** See **Bowers, A.**, 4057.
**Homer, J.** See **Foster, A. B.**, 5005.
**Hoop, G. M., and Tedder, J. M.** The direct amination of mesitylene by hydrazoic acid in concentrated sulphuric acid, 4685.
**Hooper, M.** See **Coutts, R. T.**, 5058, 5205.
**Hooton, K.** See **Glockling, F.**, 4405.
**Hopkins, L. O.** See **Cocker, W.**, 4721.
**Hopson-Hill, B. I.** See **Holt, P. F.**, 1404.
**Horler, D. F., and Nursten, H. E.** The tannins of tara, *Caesalpinia spinosa* (Mol.) Kuntze, 3786.
**Horsfield, A.** See **Clark, H. C.**, 7.
**Hough, L., and Priddle, J. E.** A bisglycerol tricarbonate, 581.
Carbonate derivatives of methyl α-D-mannopyranoside and of D-mannose, 3178.
**Hough, L., and Richardson, A. C.** Diethylsulphonyl-(2-*O*-methyl-α-D-arabopyranosyl)methane and its behaviour with base, 5561.
**Hough, L.** See also **Coxon, B.**, 1463, 1577, 1643, and **Hall, L. D.**, 1537.
**Houghton, R. P.** See **Coombs, M. M.**, 5015.
**Howard, J.** See **Austin, A. T.**, 3278, 3284, 3593.
**Howard, T. J.** See **Arcus, C. L.**, 670.
**Howell, T. E. W., Pratt, S. A. J., and Venanzi, L. M.** Some new polydentate arsenic ligands, 3167.
**Hoyle, W.** See **Belcher, R.**, 667.
**Hsu, K. K.** See **Chang, C. T.**, 3414.
**Hubert, A. J., Hargitay, B., and Dale, J.** The structure and relative stabilities of boric esters of 1,2- and 1,3-diols, 931.
**Hudec, J.** See **Cookson, R. C.**, 4499.
**Hudson, R. F.** See **Crunden, E. W.**, 3748.
**Hughes, A. N.** See **Corbett, J. F.**, 1363.
**Hughes, E. D., Ingold, Sir C., Thorpe, F. G., and Volger, H. C.** Mechanism of electrophilic substitution at a saturated carbon atom. Part IV. Kinetics, stereochemistry, and mechanism of the uncatalysed one-alkyl mercury-exchange reaction, 1133.
**Hughes, E. D., and Volger, H. C.** Mechanism of electrophilic substitution at a saturated carbon atom. Part VI. The pattern of steric effects among alkyl groups and mechanisms in one-alkyl mercury-exchange, 2359.
**Hughes, E. D.** See also **Charman, H. B.**, 1121, 1142.
**Hughes, N. A.** See **Baddiley, J.**, 2574.
**Hughes, R. B.** See **King, H. G. C.**, 3234.
**Hui, W. H.** See **Arthur, H. R.**, 551.
**Hung, M.** See **Chang, C. T.**, 3414.
**Hunt, J. H.** The resolution of chlorpheniramine and pheniramine, 2228.
**Hunter, T. F.** See **Falconer, W. E.**, 609.
**Hussey, C. W. T., and Pinder, A. R.** Investigations on the synthesis of 2-acetylcyclohex-2-enone. Part II. Some related experiments, and the constitution of the dimeric product, $C_{16}H_{22}O_4$, 3525.
**Hutchinson, D. W.** See **Clark, V. M.**, 715, 722.
**Hutchinson, M. H.** See **Coussmaker, C. R. C.**, 2705.
**Hutson, D. H., and Weigel, H.** Partial periodate oxidation of D-glucitol and its borate complex, 1546.
**Hutson, D. H.** See also **Bourne, E. J.**, 35.
**Hyne, R. A., and Tiley, P. F.** The condensed phases of sulphur trioxide. Part I. Vapour pressure and viscosity of the liquid phase at low temperatures, 2348.

XUM

I

**Ibbitson**, D. A., **James**, P. C., and **Knaust**, R. A. Dipole moments and absorption spectra of 4-arylazo-1-naphthylamines, 5163.

**Ij Aalbersberg**, W., **Gaal**, J., and **Mackor**, E. L. Electron-transfer reactions between oxygen and aromatic hydrocarbons, 905.

**Ingold**, Sir C. See **Charman**, H. B., 1121, 1142, and **Hughes**, E. D., 1133.

**Ingram**, G., and **Toms**, B. A. The reactions of sodium ethyl xanthate with ethanol and with water, 117.

**Irving**, H., and **Cox**, J. J. Studies with dithizone. Part VIII. Reactions with organometallic compounds, 1470.

**Irving**, H., and **Gillard**, R. D. A new stereospecific reaction, 2249.

**Irving**, H., and **Ramakrishna**, R. S. Studies with dithizone. Part VII. The action of halogens on dithizone and its analogues. Part IX. The absorption spectra of mono- and di-*p*-bromo-substituted dithizones and of their metal complexes, 1272, 2118.

**Irving**, H., and **Stacey**, M. H. Metal complexes of bis-[3-di(carboxymethyl)aminopropyl] ether. The computation of stability constants with the aid of a high-speed digital computor, 2019.

**Irwin**, R. S. See **Bacon**, R. G. R., 2436, 2447.

**Iskander**, Y., and **Riad**, Y. Carbon–sulphur fission in thioethers. Part IV. The mechanism of base-catalysed elimination from 4-nitrophenethylthio-derivatives of acetic, propionic, and related acids. Part VI. The structural factors leading to either carbanion–sulphenium fission or α-proton extraction in *p*-nitrophenylmethylthio-acids, 223, 2397.

**Iskander**, Y., **Riad**, Y., and **Tewfik**, R. Carbon–sulphur fission in thioethers. Part VII. Kinetics and mechanism of the carbanion–sulphenium fission in thioethers, 2402.

**Iskander**, Y., and **Tewfik**, R. Carbon–sulphur fission in thioethers. Part V. The structural factors leading to either carbanion–sulphenium fission or benzoyl elimination in (α-benzoylmethylthio)acetic acids by the action of alkalis, 2393.

**Iskander**, Y. See aso **Hanna**, S. B., 217, 221.

**Islip**, P. J. See **Ames**, D. E., 351, 4409.

**Issak**, D. See **Aroney**, M., 4148.

J

**Jackman**, L. M., and **Thompson**, D. T. Hydrogen transfer. Part XIX. Dehydrogenation of substituted 1,2-dihydronaphthalenes by quinones, and the correlation of donor reactivity with the nature of substituents, 4794.

**Jackman**, L. M. See also **Barber**, M. S., 1625, 4019, **Barton**, D. H. R., 5061, and **Elvidge**, J. A., 859.

**Jackson**, A. H. See **Abraham**, R. J., 3468.

**Jacobsen**, N. W. See **Brown**, D. J., 4413.

**Jacquignon**, P. See **Buu-Hoï**, N. P., 4836, and **Marty**, M., 384.

**James**, A. L. See **Baddiley**, J., 2574.

**James**, B. R., **Parris**, M., and **Williams**, R. J. P. Spectrophotometric and thermodynamic properties of some copper and iron complexes, 4630.

**James**, B. R., and **Williams**, R. J. P. The oxidation–reduction potentials of some copper complexes, 2007.

**James**, E. A. See **Evans**, A. G., 3532.

**James**, P. C. See **Ibbitson**, D. A., 5163.

**Jansen**, A. B. A., and **Szelke**, M. Some 4-substituted oxazoles, 405.

**Jarboe**, C. H., and **Rosene**, C. J. Volatile products of pyrolysis of nicotine, 2455.

**Jarvis**, D., **Rydon**, H. N., and **Schofield**, J. A. Polypeptides. Part VII. The synthesis and oxidation of L-cysteinyl-pentaglycyl-L-cysteine and L-cysteinyl-hexaglycyl-L-cysteine, 1752.

**Jarvis**, J. W., and **Tye**, F. L. Effect of pressure on the transport of non-electrolytes through ion-selective membranes, 4483.

**Jaques**, D., and **Leisten**, J. A. Acid-catalysed ether fission. Part I. A new mechanism, in sulphuric acid, 4963.

**Jeffery**, G. H., **Parker**, R., and **Vogel**, A. I. Physical properties and chemical constitution. Part XXXII. Thiophen compounds, 570.

**Jepson**, W. B. See **Gregg**, S. J., 884.

**John**, E. V. O. See **Goosen**, A., 4038.

**Johns**, R. B., and **Markham**, K. R. Picrotoxin and tutin. Part XII. The structure of tutin, 3006.

**Johns**, R. B. See also **Browne**, G. F., 3000.

**Johnson**, A. W., and **Kay**, I. T. The formation of porphyrins by the cyclisation of bilenes, 2418.

**Johnson**, A. W., **King**, T. J., and **Martin**, R. J. Maytenone. Part I. Isolation and structural studies, 4420.

**Johnson**, A. W., and **Tebby**, J. C. The adducts from triphenylphosphine and dimethyl acetylenedicarboxylate, 2126.

**Johnson**, A. W. See also **Crabtree**, A., 3497, and **Hill**, J. A., 4430.

**Johnson**, C. D. See **Ward**, E. R., 4314.

**Johnson**, E. A. See **Beaven**, G. H., 2749.

**Johnson**, L. F. See **Guthrie**, R. D., 4166.

**Johnston**, **A. M.** The relationship of structure to acidity in plant growth-regulating compounds. Part I. Rates of alkaline hydrolysis of substituted 2,4-dichlorophenoxyacetamides, 2335.

**Johnston**, G. A. R. See **Shoppee**, C. W., 3261.

**Jones**, A. S. See **Bayley**, C. R., 1903.

**Jones**, D. F. See **Fielding**, B. C., 4579.

**Jones**, D. N. See **Henbest**, H. B., 4472.

**Jones**, E. R. H. See **Baddeley**, G. V., 3891, **Chaudhry**, G. R., 2725, and **Gupta**, S. R., 5353.

**Jones**, J. R., and **Waters**, W. A. Oxidations of organic compounds with quinquevalent vanadium. Part VIII. The oxidation of oxalic acid, 4757.

**Jones**, J. R., **Waters**, W. A., and **Littler**, J. S. Oxidations of organic compounds with quinquevalent vanadium. Part VII. The kinetic resemblance between the oxidations of some α-hydroxy-acids and that of pinacol and of its monomethyl ether, 630.

**Jones**, K. See **Armitage**, R., 1842, and **Haslam**, E., 1829.

**Jones**, K. M. See **Holmes**, F., 4790.

**Jones**, N., and **Taylor**, H. T. Aliphatic Friedel–Crafts reactions. Part IV. The preparation of divinyl ketones, 1345.

**Jones**, N., **Taylor**, H. T., and **Rudd**, E. Aliphatic Friedel–Crafts reactions. Part III. The acylation of cycloheptane and cyclo-octene, 1342.

**Jones**, R. Alan, and **Katritzky**, A. R. Potentially tautomeric pyridines. Part III. 2-, 3-, and 4-Methanesulphonamidopyridine, 378.

**Jordan**, D. O., and **Treloar**, F. E. The cationic polymerization of styrene. Part I. The 1-phenylethyl cation. Part II. Spectra of polymerizing systems. Part III. The cocatalytic action of water in the polymerization of styrene by aluminium chloride, 729, 734, 737.

**Juneja**, H. R. See **Birch**, A. J., 5194.

K

**Kalidas**, C., and **Palit**, S. R. The activity function, $H_0$, in ethylene glycol and ethylene glycol–water mixtures, 3998.

**Kalmus**, A., and **Bergmann**, F. A simple route to 4,5-diamino-2-hydroxypyrimidine, 760.

**Kaltenbronn**, J. S. See **Büchi**, G., 2843.

**Kaluszyner**, A. See **Pelchowicz**, Z., 5418.

**Kamenar**, B., and **Grdenić**, D. The crystal structure of stannous chloride dihydrate, 3954.

**Katchalsky**, A., **Cooper**, R. E., **Upadhyay**, J., and **Wasserman**, A. Counter-ion fixation in alginates, 5198.

**Katekar**, G. F. See **Clark-Lewis**, J. W., 499.

**Katritzky**, A. R., and **Lagowski**, J. M. *N*-Oxides and related compounds. Part XVIII. Proton nuclear magnetic resonance spectra of 4-substituted pyridines and pyridine 1-oxides, 43.

**Katritzky**, A. R. See also **Cheeseman**, G. H. W., 3983, and **Jones**, R. Alan, 378.

**Kay**, I. T. See **Johnson**, A. W., 2418.

**Keay**, L., and **Crook**, E. M. The oxidation of cyclic phosphites to cyclic phosphates, 710.

**Kelly**, P., and **Smith**, M. The radiation chemistry of azide solutions. Part I. The action of *X*-rays (200 kv) on deærated aqueous solutions of sodium azide. Part II. The action of *X*-rays (200 kv) on deærated aqueous solutions of sodium azide in the presence of different organic solutes, 1479, 1487.
**Kemball**, C. See **Madden**, W. F., 302.
**Kemmitt**, R. D. W., and **Sharp**, D. W. A. The preparation of complex fluorides by use of sulphur tetrafluoride as fluorinating agent, 2496.
**Kempa**, R. F., and **Lee**, W. H. Physicochemical studies of some cyclic carbonates. Part III. Electrical conductivities in ethylene carbonate, 100.
**Kendall**, J. D. See **Ficken**, G. E., 584, 747.
**Kennard**, C. H. L. See **Barclay**, G. A., 3289, 5244.
**Kennedy**, J., **Lewis**, A., **McCorkindale**, N. J., and **Raphael**, R. A. Synthesis of (±)-*cis*-9-hydroxyoctadec-12-enoic acid, 4945.
**Kennedy**, J., **McCorkindale**, N. J., and **Raphael**, R. A. A new synthesis of queen substance, 3813.
**Kennedy**, M. See **Tyrrell**, H. J. V., 3432.
**Kenner**, G. W. See **Abraham**, R. J., 3468.
**Kepert**, D. L. See **Duncan**, J. F., 5317.
**Kerridge**, K. A. See **Davoll**, J., 2589.
**Kertes**, A. S., and **Beck**, A. Solvent-extraction of septivalent rhenium. Part I. Heterogeneous equilibria in the system, aqueous nitric acid–potassium perrhenate–tributyl phosphate. Part II. Heterogeneous equilibria in the system, aqueous nitric acid–potassium perrhenate–"tri-iso-octylamine." Part III. Heterogeneous equilibria in the system, aqueous nitric acid–potassium perrhenate–dibutyl phosphate, 1921, 1926, 5046.
**Kettle**, S. F. A. The kinetics of the decomposition of stannane on a tin surface, 2569.
**Kidd**, D. A. A. The characterisation of amines by use of (−)-di-*O*-*p*-toluoyltartaric acid, 4675.
**Kilner**, M. See **Addison**, C. C., 4839.
**Kimber**, R. W. L. See **Badger**, G. M., 3407.
**Kimchi**, D., and **Bien**, S. Synthetic and stereochemical studies in the perhydrobenzocyclohepten-1-one system, 5345.
**Kincl**, F. A. See **Bowers**, A., 4057.
**King**, E. J., and **Prue**, J. E. Precise measurements, with the glass electrode, of the ionization constants of benzoic, phenylacetic, and β-phenylpropionic acids at 25°, 275.
**King**, F. E., **King**, T. J., and **Read**, G. Some potential intermediates for the synthesis of diterpenes, 960.
**King**, F. E. See also **Covell**, C. J., 702, and **Cross**, A. D., 2714.
**King**, G. The rôle of peroxides in the autoxidation of elaidic acid and oleic esters, 4324.
**King**, H. G. C., and **White**, T. Trigallic acid, a probable component of tannic acid, 3231.
The colouring matter of *Rhus cotinus* wood (young fustic), 3538.
The reaction of certain $C_{15}$ compounds with acetic anhydride–sulphuric acid, 3539.
**King**, H. G. C., **White**, T., and **Hughes**, R. B. The occurrence of 2-benzyl-2-hydroxycoumaran-3-ones in Quebracho tannin extract, 3234.
**King**, N. J. See **Anderson**, D. M. W., 2914, 5230, 5333.
**King**, T. J., and **Read**, G. Tanshinones. Part I. The synthesis of an isomer of tanshinone-I, 5090.
**King**, T. J., and **Yardley**, J. P. The structure of bassic acid, 4308.
**King**, T. J. See also **Cross**, A. D., 2714, **Elmore**, N. F., 4425, **Hill**, J. A., 4430, **Johnson**, A. W., 4420, and **King**, F. E., 960.
**Kingston**, D. See **Glockling**, F., 4405.
**Kirby**, E. C., and **Reid**, D. H. Conjugated cyclic hydrocarbons and their heterocyclic analogues. Part IV. Dimethinecyanine salts from 1-formylazulenes and heterocyclic quarternary ammonium salts. Part V. 1-1′-Azulenylmethyleneazulenium salts and 1-ethoxymethyleneazulenium salts. Part VI. The condensation of azulenes with aliphatic aldehydes in the presence of perchloric acid, 163, 1724, 3579.
**Kirby**, G. W. See **Clark**, V. M., 715.
**Kirk**, D. N., and **Petrow**, V. Modified steroid hormones. Part XXI. 17β-Hydroxy-11-methylene- and -11β-methyl-5α-androstan-3-one, 2091.
**Kirk**, D. N., **Petrow**, V., and **Williamson**, D. M. Modified steroid hormones. Part XXII. 6α,16α-Dimethylprogesterone and 17α-acetoxy-6α-methyl-16-methyleneprogesterone, 2821.
**Kirkien-Konasiewicz**, A. The solvolysis of 7-phenyltetronic acid enol esters. Part II. The methanolysis of γ-phenyltetronic acid enol acetate, 5430.
**Kirkien-Konasiewicz**, A., and **Maccoll**, A. The mechanism of solvolysis of γ-phenyltetronic acid enol esters. Part I. A conductometric study of the methanolysis of γ-phenyltetronic acid enol benzoate, 5421.
**Kläning**, U., and **Symons**, M. C. R. Structure and reactivity of the oxyanions of transition metals. Part XI. Ultraviolet spectra of monosubstituted chromate ions, 3204.
**Klassen**, N. V. See **Beaven**, G. H., 2749, and **de la Mare**, P. B. D., 5285.
**Klibansky**, Y. See **Sondheimer**, F., 767.
**Klyne**, W., and **Marshall-Jones**, P. Optical rotatory dispersion. Part II. 3-Monohydroxy-steroids, 3,17-dihydroxy-steroids, and their derivatives, 5415.
**Klyne**, W. See also **Sondheimer**, F., 767.
**Knaust**, R. A. See **Ibbitson**, D. A., 5163.
**Knight**, J. C. See **Dean**, F. M., 327.
**Knights**, B. A. See **Ansell**, M. F., 212, 2903.
**Knowles**, J. R., and **Norman**, R. O. C. The transmission of polar effects through aromatic systems. Part II. The nitration of benzyl derivatives, 2938.
The *ortho* : *para*-ratio in aromatic substitution. Part V. Nitration by mixed acid and acetyl nitrate, 3888.
**Knowles**, P. F. See **Haslam**, E., 1854.
**Knox**, G. R., **Munro**, J. D., **Pauson**, P. L., **Smith**, G. H., and **Watts**, W. E. Some substituted cyclopentadienyl derivatives of nickel, cobalt, iron, molybdenum, and titanium, 4619.
**Knox**, G. R., and **Pauson**, P. L. Ferrocene derivatives. Part X. Their preparation from fulvenes. Part XI. Azoferrocenes, 4610, 4615.
**Knox**, J. H. The speed of analysis by gas chromatography, 433.
**Knox**, J. H. See also **Falconer**, W. E., 782, 4285, and **Grzybowska**, B., 4402.
**Koenigsberger**, R. See **de la Mare**, P. B. D., 5285.
**Kohnstam**, G. See **Brittain**, E. F., 2045.
**Kolker**, P. L. See **Bokadia**, M. M., 4663.
**Kosolapoff**, G. M., and **Struck**, R. F. Diphosphine dioxides. Part II. Some diphosphine dioxides with mono-, di-, and tri-methylene bridges, 2423.
**Krishna**, B., and **Tewari**, K. C. Kinetics and mechanism of oxidation of mandelic, DL-malic, and lactic acid by ceric sulphate, 3097.
**Krueger**, G. See **Shoppee**, C. W., 3641.
**Kugel**, L. See **Halmann**, M., 3542.
**Kulczycka**, A. See **Gray**, C. H., 2264, 2268, 2276.
**Kurzer**, F. Thiadiazoles. Part XI. Synthesis and cyclisation of *N*-(thiobenzamido)guanidines and related compounds, 1617.
**Kurzer**, T. See also **Godfrey**, L. E. A., 5137.
**Kynaston**, W. See **Evans**, R. F., 5556.

## L

**Labib**, A. See **El-Abbady**, A. M., 1083.
**Lack**, R. E. See **Shoppee**, C. W., 1311, 2291, 3271.
**Lagowski**, J. M. See **Forrest**, H. S., 43, 963.
**Laird**, R. M. See **Addy**, J. K., 1708.
**Laird**, W., **Spring**, F. S., and **Stevenson**, R. Triterpenoids. Part LVIII. The synthesis of isoursenol, the ursane analogue of taraxerol, 2638.
**Lamberton**, A. H., and **Newton**, G. Nitramines and nitramides. Part XII. The base-catalysed decomposition of some *ON*-dialkylnitramines, and evidence for the existence of geometrical isomers, 1797.
**Land**, E. J., and **Porter**, G. A stable anilino-radical, 3540.
**Lansbury**, R. C. See **Alner**, D. J., 3169.
**Lapidot**, A. See **Halmann**, M., 3158.
**Lappert**, M. F. Co-ordination compounds having carboxylic esters as ligands. Part I. Stoicheiometry, structure, and stereochemistry, 817.

**Lappert, M. F.**, and **Smith, J. K.** Reactions of sulphoxides with some Group III and IV halides, 3224.
**Lappert, M. F.** See also **Aubrey, D. W.**, 1931.
**Large, D. G.**, **Rydon, H. N.**, and **Schofield, J. A.** Polypeptides. Part VI. A further study of the oxidation of L-cysteinyl-tetraglycyl-L-cysteine, 1749.
**Larkin, J. A.**, and **McGlashan, M. L.** A new calorimeter for heats of mixing. The heat of mixing of benzene with carbon tetrachloride, 3425.
**Larkworthy, L. F.** Iron bisindigo, a compound reported to exhibit oxygen-carrying properties, 4025.
**Law, H. D.**, **Millar, I. T.**, and **Springall, H. D.** The structure of evolidine, 279.
**Lawley, P. D.** See **Brooks, P.**, 3923.
**Lawrie, W.** See **Allison, J. M.**, 3353, 5224.
**Lawson, A.** See **Adcock, B.**, 5120.
**Leaback, D. H.** See **Greig, C. G.**, 879.
**Leaver, D.** See **Miller, W.**, 4485.
**Leckey, R. G.** See **Hamer, D.**, 1398.
**Ledwith, A.** See **Bradley, J. N.**, 1495.
**Lee, W. H.** See **Kompa, R. F.**, 100.
**Leese, C. L.**, and **Timmis, G. M.** 1-Aminoimidazoles and derivatives. Part I. The synthesis of 1-amino-derivatives of 5-amino-2-methylimidazole-4-carboxamide, 3816. Potential anti-purines. Part IV. The synthesis of 9-dimethylaminopurines, 3818.
**Le Fèvre, C. G.** See **Cureton, P. H.**, 4447.
**Le Fèvre, R. J. W.**, and **Williams, A. J.** Molecular polarisability. Chloroform as a solvent for the determination of molar Kerr constants of solutes, 1671.
**Le Fèvre, R. J. W.** See also **Aroney, M.**, 4140, 4144, 4148, **Cureton, P. H.**, 4447, **Eckert, J. M.**, 2356, and **Hacket, N.**, 2612.
**Lehmann, J.** See **Foster, A. B.**, 4649, 5005, 5011.
**Leigh, G. J.** See **Beattie, I. R.**, 4249.
**Leigh, W. R. D.** Fission of triphenylmethyl derivatives of secondary cellulose acetates by hydrogen bromide, 754.
**Leisten, J. A.** Cyclic anhydrides in sulphuric acid, 2191.
**Leisten, J. A.** See also **Jaques, D.**, 4963.
**Lele, S. S.**, **Patel, M. G.**, and **Sethna, S.** Synthesis of some bicoumarinyl and 8-phenylcoumarin derivatives, 969.
**Lenthen, P. M.** See **Aroney, M.**, 4140, and **Wren, J. J.**, 2557.
**Leonard, J. A.** See **Hey, D. H.**, 232.
**Lesslie, M. S.**, and **Mayer, U. J. H.** Optical studies of 2,2′-di-t-butylbiphenylcarboxylic acids and of 2′-t-butylbiphenyl-2-carboxylic acid, 611.
**Letters, R.**, and **Michelson, A. M.** $O^2$,3′-Cyclouridine, 1410.
**Letters, R.** See also **Brown, D. M.**, 3774.
**Lever, A. B. P.** See **Elvidge, J. A.**, 1257.
**Lewin, N.** See **Birnbaum, H.**, 1224.
**Lewis, A.** See **Kennedy, J.**, 4945.
**Lewis, D.** See **Gray, G. W.**, 1069, 5156.
**Lewis, D. G.** See **Edwards, R. L.**, 4995.
**Lewis, J.**, **Nyholm, R. S.**, and **Smith, P. W.** The structure of complex molybdenum(III) thiocyanates, 4590.
**Lewis, J.** See also **Barraclough, C. G.**, 2582, 2601, **Earnshaw, A.**, 369, 3132, **Figgis, B. N.**, 3138, and **Griffith, W. P.**, 775, 2259.
**Lewis, J. R.** See **Hassall, C. H.**, 2312.
**Lewis, K. G.** Triterpene constituents of the fruits of the osage orange (*Maclura pomifera*). Part II. Synthesis of the natural diol, lupane-3β,20-diol, 2330.
The reaction between furfuryl alcohol and 2,4-dinitrophenylhydrazine in methanolic hydrochloric acid, 4690.
**Liddle, A. M.** See **Archibald, A. R.**, 1183, and **Corbett, W. M.**, 531.
**Liljegren, D. R.**, and **Potts, K. T.** 1,2,4-Triazoles. Part II. 3-Alkyl-5-aryl-1,2,4-triazoles, 518.
**Liljegren, D. R.** See also **Hart, G.**, 4267.
**Lilly, M. N.** See **Eaborn, C.**, 3052.
**Lingard, R. G.** See **Beckett, A. H.**, 588.
**Linnett, J. W.** The structure of $(PW_{12}O_{40})^{3-}$ and related ions, 3796.
**Linnett, J. W.** See also **Barber, M.**, 3323.
**Lister, J. H.** See **Clark, J.**, 5048.
**Littler, J. S.** See **Jones, J. R.**, 630.
**Livingstone, J. G.** See **Coates, G. E.**, 1000, 4909, 5053.
**Llewellyn, D. R.** See **Barnard, P. W. C.**, 2670, and **Bunton, C. A.**, 1636.
**Loewenthal, H. J. E.** Syntheses in the colchicine series. Part III. The disposition of the oxygen functions in colchicine, 1421.
**Loewenthal, H. J. E.**, and **Rona, P.** Syntheses in the colchicine series. Part IV. Structural and conformational aspects in some fused seven-membered ring systems, 1429.
**Loh, L. Y. S.** See **Arthur, H. R.**, 4360.
**Long, A. G.** See **Carrington, T. R.**, 4560, **Green, G. F. H.**, 2532, and **Gregory, G. I.**, 3059.
**Long, R.** See **Biddulph, R. H.**, 1822.
**Love, C. W.** See **Bokadia, M. M.**, 4663.
**Loveluck, G. D.** Dipole moment studies on polyethylene and polypropylene glycols of low molecular weight, 4729.
**Lovie, J. C.**, and **Thomson, R. H.** Naturally occurring quinones. Part IV. A synthesis of alaternin, 485.
**Lowe, G.** See **Gardner, J. N.**, 1532.
**Lowry, J. B.** See **Briggs, L. H.**, 642.
**Lucaszewski, G. M.**, **Redfern, J. P.**, and **Salmon, J. E.** Arsenates. Part I. Preparative, phase-diagram, and other preliminary studies of the system chromium(III)–arsenic acid, 39.
**Lucken, E. A. C.**, and **Whitehead, M. A.** Chemical applications of nuclear quadrupole resonance. Part IV. The transmission of the electronic effect of various substituents by a phosphorus atom, 2459.
**Lucken, E. A. C.** See also **Brandon, R. W.**, 4273.
**Lunt, E.** See **Barber, H. J.**, 2828.
**Lyons, L. E.** See **Casimir, D. J.**, 5297.

M

**Mabbs, F. E.** See **Figgis, B. N.**, 3138.
**Mabille, P.**, and **Buu-Hoï, N. P.** 12-Benzyl- and 12-alkyl-6-aminochrysenes, 4911.
**McAuley, A.**, and **Nancollas, G. H.** Thermodynamics of ion association. Part VII. Some transition-metal oxalates. Part IX. Some transition-metal succinates, 2215, 4458.
**McCleverty, J. A.** See **Green, M. L. H.**, 4854.
**Maccoll, A.**, and **Stone, R. H.** Gas-phase eliminations. Part II. The pyrolysis of s-butyl chloride, and the direction of eliminations from s-butyl compounds, 2756.
**Maccoll, A.** See also **Kirkien-Konasiewicz, A.**, 5421.
**McCorkindale, N. J.** See **Kennedy, J.**, 3813, 4945.
**McCrea, P. A.** See **Baker, J. A.**, 3854.
**MacDiarmid, A. G.** See **Chamberland, B. L.**, 445.
**MacDuffie, D. E.** See **Emeléus, H. J.**, 2597.
**McEntee, J.** See **Henbest, H. B.**, 4478.
**McGeachin, H. M.**, and **Tromans, F. R.** Phosphonitrilic derivatives. Part VII. The crystal structure of tetrameric phosphonitrilic fluoride, 4777.
**McGee, J.**, and **Ritchie, P. D.** Studies in pyrolysis. Part XVI. Pyrolysis of some open-chain α-anilino-carboxylic acids, 1782.
**McGhie, J. F.** See **Barton, D. H. R.**, 1215.
**McGlashan, M. L.** See **Larkin, J. A.**, 3425.
**McGowan, C. R.** See **Spice, J. E.**, 3021.
**McGowan, J. C.**, and **Powell, T.** Reactions of αα-diphenyl-β-picrylhydrazyl with phenols, 2160.
**Machell, G.**, and **Richards, G. N.** Methylglucosides as transfer agents in polymerisation of acrylonitrile and styrene, 3308.
**McIntyre, J. E.**, and **Ravens, D. A. S.** The oxidation of alkylaromatic compounds in aqueous hydrogen bromide, 4082.
**McKay, J. E.** See **Corbett, W. M.**, 2930, 5041.
**Mackay, K. M.** See **Emeléus, H. J.**, 2676.
**McKay, R. B.** See **Giles, C. H.**, 58, 5434.
**Mackie, I. M.**, and **Percival, E.** Polysaccharides from the green seaweeds of *Caulerpa* spp. Part III. Detailed study of the water-soluble polysaccharides of *C. filiformis*: comparison with the polysaccharides synthesised by *C. racemosa* and *C. sertularioides*, 3010.
**Mackie, R. K.** See **Champion, N. G. S.**, 5060.
**McKinnon, D. M.** See **Hogg, W.**, 1403.
**Mackor, E. L.** See **Aalbersberg, W. Ij.**, 905.
**McLean, J.** See **Allison, J. M.**, 3353, 5224.
**McLoughlin, V. C. R.** See **Bourne, E. J.**, 1771.
**McMeekin, W.** See **Bladon, P.**, 3504.

**McMorris**, T. C. See **Barton**, D. H. R., 2027.
**McMurry**, T. B. H. See **Cocker**, W., 4721.
**McNae**, C. J. See **Holt**, P. F., 1404, 1825.
**McNeil**, D. See **Copeland**, P. G., 1232, 3858, 3864, and **Dean**, R. E., 2773.
**McNeill**, I. C. A convenient method for the preparation of [$^{36}$Cl]chlorine from [$^{36}$Cl]hydrochloric acid: decomposition of palladous [$^{36}$Cl]chloride, 639.
**McOmie**, J. F. W. See **Baker**, W., 479, 2965, 2971, 3986.
**McQuillan**, A. H. See **Miller**, W., 4485.
**MacWilliam**, I. C. See **Harris**, G., 2053.
**Madden**, W. F., and **Kemball**, C. Catalysis with evaporated metal films in a flow system. Part I. The hydrogenation of benzene and cyclohexene over nickel, 302.
**Magrill**, D. S. See **Brooks**, C. J. W., 308.
**Maitland**, P. See **Bethell**, J. R., 5211.
**Maitlis**, P. M. New heteroaromatic compounds. Part IX. Some 10,9-borazaroanthracenes, 425.
The preparation of *o*-(4-phenylbuta-1,3-dienyl)phenylboronic anhydride, 3149.
**Makinson**, G. K. See **Haslam**, E., 5153.
**Malpass**, V. E. See **Davies**, M., 1048.
**Mandleberg**, C. J., and **Davies**, D. The vapour pressure of plutonium tetrafluoride, 2031.
**Mandleberg**, C. J., **Francis**, K. E., and **Smith**, R. The solubility of plutonium trifluoride, plutonium tetrafluoride, and plutonium(IV) oxalate in nitric acid mixtures, 2464.
**Mann**, B. R. See **Fischer**, A., 1093.
**Mann**, F. G., and **Baker**, F. C. The double methopicrates of certain heterocyclic tertiary amines, 3845.
**Mann**, F. G. See also **Forbes**, M. H., 2762, and **Hinton**, R. C., 5454.
**Manners**, D. J., and **Wright**, A. α-1,4-Glucosans. Part XII. End-group assay of glycogens by oxidation with sodium metaperiodate, 2681.
**Manners**, D. J. See also **Archibald**, A. R., 1183.
**Manning**, M. See **Finar**, I. L., 2733.
**Markham**, K. R. See **Browne**, G. F., 3000, and **Johns**, R. B., 3006.
**Markin**, T. L. See **Bagnall**, K. W., 1611.
**Marks**, G. S., and **Neuberger**, A. Synthetic studies relating to the carbohydrate–protein linkage in egg albumin, 4872.
**Marsden**, F. J. See **Feeney**, J., 356, and **Holliday**, A. K., 3348.
**Marshall**, B. A., and **Waters**, W. A. Oxidations of organic compounds by cupric salts. Part II. The oxidation of benzoin, 1579.
**Marshall-Jones**, P. See **Klyne**, W., 5415.
**Martin**, E. C. The distribution of water and butan-1-ol on chromatograms made by the ascending technique, 3935.
**Martin**, G. C., **Parkyns**, N. D., and **Ubbelohde**, A. R. Electron-donor and -acceptor complexes with aromatic systems. Part VIII. Preparations and physical measurements of new metal addition complexes with aromatic systems in the solid state, 4958.
**Martin**, G. C., and **Ubbelohde**, A. R. Electron-donor and -acceptor complexes with aromatic systems. Part VII. Electron-donor and -acceptor complexes of some tetracyclic aromatic and heteroaromatic molecules, 4948.
**Martin**, R. J. See **Johnson**, A. W., 4420.
**Martin**, R. L., and **Winter**, G. The association of n-tetraalkoxy- and n-alkoxy-chloro-derivatives of titanium, 2947.
**Martin-Smith**, M. See **Barton**, D. H. R., 5061.
**Martlew**, E. F. See **Foster**, A. B., 1204.
**Marty**, M., **Buu-Hoï**, N. P., and **Jacquignon**, P. Carcinogenic nitrogen compounds. Part XXIX. 2,5-Diethylaniline and benzacridines derived therefrom, 384.
**Mason**, R. See **Craig**, D. P., 1376.
**Massey**, A. G. The reactions of boron chlorides with acetone, 1103.
**Massey**, A. G., and **Holliday**, A. K. The reaction of diboron tetrachloride with ethylene oxide, 1893.
**Massey**, A. G., and **Packer**, K. J. Some reactions of sulphur chloride pentafluoride, 5554.
**Massey**, A. G. See also **Holliday**, A. K., 3348.
**Masui**, M., and **Sayo**, H. Controlled-potential electrolysis. Part VI. Reductions of 2,2-dinitropropane. Part VII. Polarographic behaviour and controlled-potential electrolysis of 1,1-dinitroethane and dinitromethane, 4773, 5325.
**Masui**, M., **Tsuda**, Y., and **Yijima**, C. *NN*-Di-(1-cyanoalkyl)-hydroxylamines. Part I. The preparation of *NN*-di-(1-cyanoalkyl)hydroxylamines, 4063.
**Mateescu**, G. See **Balaban**, A. T., 3564.
**Mather**, J. G., and **Shorter**, J. The cumulative effect of substituents in an aromatic nucleus on reactions of the side-chain: the effect of chlorine as substituent on the reaction of benzoyl chlorides with aniline, on the alkaline hydrolysis of ethyl benzoates, and on the ionisation of benzoic acids, 4744.
**Mathur**, K. B. L., and **Mehra**, H. S. Arylation of 2-furoic acid in Meerwein's diazo-reaction, 2576.
**Matsuura**, S. See **Albert**, A., 5131.
**Mattocks**, A. R., **Schoental**, R., **Crowley**, H. C., and **Culvenor**, C. C. J. Indicine: the major alkaloid of *Heliotropium indicum* L., 5400.
**Mattocks**, A. R. See also **Heath**, D. F., 4226.
**Maxted**, E. B., and **Ali**, S. I. The rôle of supports in catalytic hydrogenation. Part I. Activation effects of various oxide carriers on palladium, 4137.
**Maxted**, E. B., and **Elkins**, J. S. The rôle of supports in catalytic hydrogenation. Part II. Further effects of various oxide supports on the activity of platinum, 5086.
**Mayer**, U. J. H. See **Lesslie**, M. S., 611.
**Mays**, M. J. See **Ebsworth**, E. A. V., 4879.
**Meakins**, G. D., and **Pemberton**, M. W. Steroids of unnatural configuration. Part VI. Oxidation and reduction of epilumisterol, 4676.
**Meakins**, G. D. See also **Dalton**, F., 1880.
**Mehra**, H. S. See **Mathur**, K. B. L., 2576.
**Mehrotra**, R. C., and **Srivastava**, G. Organic derivatives of boron. Part II. Catechol derivatives, 4045.
**Mehta**, M. D. See **Brain**, E. G., 633.
**Meinwald**, Y. See **Banks**, B. E. C., 3240.
**Mellor**, J. R. See **Coussmaker**, C. R. C., 2705.
**Mercer**, G. A. See **Archibald**, A. R., 1183.
**Merchant**, J. R. See **Vaghani**, D. D., 1066.
**Meshreki**, M. H. See **El Khadem**, H., 2957.
**Michalski**, J., **Modro**, T., and **Zwierzak**, A. Anhydrides of organophosphorus acids. Part II. The synthesis of tri- and tetra-alkyl esters of phosphorous phosphoric anhydride, 4904.
**Michelson**, A. M. See **Letters**, R., 1410.
**Midgley**, A. See **Dean**, R. E., 2773.
**Mijović**, M. P. V., and **Walker**, J. Chemistry of micrococcin *P*. Part V. The infrared absorption spectra of thiazoles, 3381.
**Mijović**, M. P. V. See also **Dean**, B. M., 3394.
**Miles**, D. H. See **Adcock**, B., 5120.
**Millar**, I. T. See **Forbes**; M. H., 2762, and **Law**, H. D., 279.
**Millen**, D. J., and **Pannell**, J. The microwave spectrum, structure, and nuclear quadrupole coupling coefficients of nitrosyl chloride, 1322.
**Miller**, D. B. See **Finar**, I. L., 2769.
**Miller**, J. R. Metal–metal interactions in square-planar complexes, 4452.
**Miller**, J. R., and **Sharpe**, A. G. The structure of disalicylaldehydenickel, 2594.
**Miller**, R. E., and **Wynne-Jones**, W. F. K. Complex formation in pyridine solutions of aromatic polynitro-hydrocarbons, 4886.
**Miller**, R. E. See also **Dodd**, R. E., 2790.
**Miller**, W., **Stafford**, W. H., **Taylor**, W. H., **Leaver**, D., and **McQuillan**, A. H. Radiation chemistry of organic halogen compounds. Part I. The action of γ-radiation on chlorinated ethylenes, 4485.
**Milligan**, B., **Saville**, B., and **Swan**, J. M. New syntheses of trisulphides, 4850.
**Milligan**, B., **Spinner**, E., and **Swan**, J. M. The infrared spectra of some oxamides and thio-oxamides, 1919.
**Milligan**, B., and **Swan**, J. M. Synthesis of thio-oxamides and thioamides by extensions of the Kindler reaction, 1194.
Condensation of phenacyl thiolsulphates with diazonium salts, 4266.
Reactions of sodium 2-oxocyclohexyl thiolsulphate, 5552.
**Mills**, B., and **Schofield**, K. Indoles. Part VI. Some dioxindoles and their conversion into *o*-aminoaryl ketones, 5558.

**Mills**, H. H. See **Speakman**, J. C., 1164.
**Mills**, S. D. See **Haslam**, E., 1836.
**Mishra**, H. C. See **Arotsky**, J., 12.
**Modro**, T. See **Michalski**, J., 4904.
**Moelwyn-Hughes**, E. A. The kinetics of the hydrolysis of t-butyl chloride, 1517.
**Moelwyn-Hughes**, E. A. See also **Farhat-Aziz**, 1523.
**Money**, T., **Raphael**, R. A., **Scott**, A. I., and **Young**, D. W. An alternative synthetic approach to (±)-gibberone, 3958.
**Monk**, C. B. See **Atkins**, V. M., 1817, and **Morgans**, D. E. B., 1819.
**Monks**, E. R. See **French**, C. M., 466.
**Montgomery**, A. J. See **Finar**, I. L., 367.
**Mooney**, E. F. See **Gerrard**, W., 3153, 4255.
**Moore**, R. H. See **Bailey**, A. J., 4086.
**Morgan**, D. J. See **Browning**, M. C., 4816.
**Morgan**, J. W. W. See **Covell**, C. J., 702.
**Morgan**, K. See **Peat**, S., 623.
**Morgan**, K. J. Infrared spectra and structure of arylazonaphthols, 2151.
The infrared spectra of some simple benzimidazoles, 2343.
**Morgans**, D. E. B., and **Monk**, C. B. The adsorption of uranyl sulphate from 20% methanol by an anion-exchange resin, 1819.
**Morley**, J. S. Preparation of polychlorobenzylamines, 1414.
**Morman**, J. F. See **Bellamy**, L. J., 4762, and **Brooks**, C. J. W., 661, 3372.
**Morris**, D. F. C., and **Short**, E. L. Manganese(II) chloride complexes. Part I. Stability constants, 5148.
**Morrison**, A. See **Cross**, B. E., 2498.
**Mortimer**, C. T. See **Fowell**, P. A., 3793.
**Mortimer**, P. I. See **Clark-Lewis**, J. W., 189, 499, 4268.
**Morton**, R. A. See **Belić**, I., 2523.
**Moser**, W. See **Donaldson**, J. D., 835, 839, 1996.
**Moulden**, H. N. See **Burn**, A. J., 5542, and **Cadogan**, J. I. G., 3079, 5524.
**Moye**, C. J. See **Birch**, A. J., 4691.
**Moynehan**, T. M. See **Hey**, D. H., 232.
**Mukherjee**, R. N. See **Goldwhite**, H., 3825.
**Munday**, L. Amino-acids of the cyclohexane series. Part I, 4372.
**Munro**, D. O. Physicochemical properties of some chemotherapeutic thioxanthones, 5381.
**Munro**, J. D., and **Pauson**, P. L. Cycloheptatriene– and tropylium–metal complexes. Part I. The "normal" reaction of tricarbonyltropyliumchromium salts with anions. Part II. The rearrangement to benzene complexes. Part III. The "abnormal" reaction with anions, 3475, 3479, 3484.
**Munro**, J. D. See also **Knox**, G. R., 4619.
**Murphy**, J., **Roubinek**, L., and **Wassermann**, A. Mechanism of formation of a deeply coloured electrically conducting polymer, 1964.
**Murrell**, J. N. See **Cromartie**, R. I. T., 2063.
**Musgrave**, W. K. R. See **Chambers**, R. D., 3779.

N

**Nabney**, J. See **Day**, A. C., 4067.
**Nair**, V. S. K., and **Nancollas**, G. H. Thermodynamics of ion association. Part VIII. Some transition-metal malonates, 4367.
**Nakhwa**, S. N. See **Giles**, C. H., 93.
**Namkung**, M. J. See **Fletcher**, T. L., 1400.
**Nánási**, P., and **Bognár**, R. Preparation of isomeric *N*-arylglycosylamines, 323.
**Nánási**, P. See also **Bognár**, R., 320.
**Nancollas**, G. H. See **McAuley**, A., 2215, 4458, and **Nair**, V. S. K., 4367.
**Nasipuri**, D. Polycyclic systems. Part X. Structure of the $C_{28}$ hydrocarbon from cholesterol: a synthesis of 4′-isobutyl-6′-methylindeno(2′,3′ : 1,2)phenanthrene, 4230.
**Nasipuri**, D., and **Roy**, D. N. Polycyclic systems. Part IX. A new synthesis of indeno(2′,3′ : 1,2)phenanthrene, 3361.
**Naylor**, R. N., **Shaw**, G., **Wilson**, D. V., and **Butler**, D. N. Purines, pyrimidines, and imidazoles. Part XVI. Some 1-aminoimidazoles and derived 9-aminopurines, 4845.
**Necoechea**, E. See **Bowers**, A., 4057.
**Neilson**, D. G. See **Roger**, R., 3181.
**Neilson**, T. See **Cresswell**, R. M., 476.
**Nenitzescu**, C. D. See **Balaban**, A. T., 3553, 3561, 3564, 3566.
**Nery**, R. See **Boyland**, E., 679.
**Neuberger**, A. See **Marks**, G. S., 4872.
**Neumann**, F. See **Bowers**, A., 1859.
**Newbold**, B. T. Reduction of iodonitrobenzenes, 4260.
**Newbold**, G. T. See **Currie**, A. C., 4693.
**Newbould**, J. See **Bokadia**, M. M., 4663, and **Brown**, B. R., 3677.
**Newitt**, E. J. See **Burgess**, A. R., 1884.
**Newman**, G., and **Powell**, D. B. The infrared spectra and structures of the complexes dichloro(ethylenediamine)-zinc, -cadmium, and -mercury, 477.
**Newns**, G. R. See **Hickling**, A., 5177, 5186.
**Newton**, G. See **Lamberton**, A. H., 1797.
**Ng**, Y. L. See **Arthur**, H. R., 3551.
**Nicholls**, D. See **Fowles**, G. W. A., 95.
**Nicholson**, D. C. See **Gray**, C. H., 2264, 2268, 2276.
**Nisbet**, M. A. See **Cocker**, W., 4721.
**Nixon**, P. See **Clifford**, B., 3516.
**Norman**, R. O. C., and **Radda**, G. K. The *ortho* : *para*-ratio in aromatic substitution. Part I. The nitration of methyl phenethyl ether. Part III. A general discussion, 3030, 3610.
**Norman**, R. O. C., **Radda**, G. K., **Brimacombe**, D. A., **Ralph**, P. D., and **Smith**, E. M. The transmission of polar effects through aromatic systems. Part III. Hammett σ-constants, 3247.
**Norman**, R. O. C., and **Ralph**, P. D. The transmission of polar effects through aromatic systems. Part I. Substituted anthracenes, 2221.
**Norman**, R. O. C. See also **Billing**, C. J., 3885, **Harvey**, D. R., 3604, and **Knowles**, J. R., 2938, 3888.
**Novotny**, J. See **Badger**, G. M., 3400, 3403.
**Nursten**, H. E. See **Horler**, D. F., 3786.
**Nyholm**, R. S. See **Barclay**, G. A., 4433, **Barraclough**, C. G., 2582, and **Lewis**, J., 4590.
**Nyman**, F. See **Haszeldine**, R. N., 3015.

O

**O'Kelly**, J., and **Sargeant**, K. Supinine from the seeds of *Trichodesma zeylanicum*, R. Br, 484.
**Øksne**, S. See **Cheeseman**, G. H. W., 3983.
**Olavesen**, A. H. See **Foster**, A. B., 5095.
**Oliver**, T. Isopropenyl and isopropylidene groups: the terpene problem, 2353.
**Ollis**, W. D. See **Djerassi**, C., 1448.
**Openshaw**, H. T., and **Whittaker**, N. The synthesis of emetine and related compounds. Part III. The reaction of some isoquinoline derivatives with acrylonitrile, 4939.
**Orchin**, M. See **Garcia**, L., 2254.
**Orgel**, L. E. Double bonding in chelated metal complexes, 3683.
**Orhanović**, M. See **Asperger**, S., 2142.
**Orman**, S. See **Hambling**, J. K., 3108, and **Hey**, D. H., 565.
**Osbond**, J. M. Chemical constitution and amœbicidal activity. Part VI. A new synthesis of 2-ketones and 2-alcohols derived from 3-alkyl-1,3,4,6,7,11b-hexahydro-9,10-dimethoxy-2*H*-benzo[*a*]quinolizines, 4711.
Essential fatty acids. Part II. Synthesis of (±)-vernolic, linoleic, and γ-linolenic acid, 5270.
**Osbond**, J. M., **Philpott**, P. G., and **Wickens**, J. C. Essential fatty acids. Part I. Synthesis of linoleic, γ-linolenic, arachidonic, and docosa-4,7,10,13,16-pentaenoic acid, 2779.
**Osborn**, A. J. See **Greenwood**, N. N., 1775.
**Osgerby**, J. M., and **Pauson**, P. L. Ferrocene derivatives. Part VIII. Tetrahydropyridoferrocenes. Part IX. Some disubstituted derivatives, 4600, 4604.
**Oughton**, J. F. See **Attenburrow**, J., 4547, **Bailey**, E. J., 4535, and **Elks**, J., 4531.
**Overend**, W. G., **Peacocke**, A. R., and **Smith**, J. B. Reaction at position 1 of carbohydrates. Part I. The polarographic reduction of carbohydrates, 3487.
**Overend**, W. G. See also **Capon**, B., 5172.
**Overton**, K. H. See **Connolly**, J. D., 3366.

**Owen**, A. J. The pyrolysis of decaborane, 5438.
**Owen**, E. D. See **Evans**, A. G., 3532.
**Owen**, G. D. T. See **Evans**, A. G., 1733.
**Owen**, L. N. See **Benn**, M. H., 2365, and **Creighton**, A. M., 2375.
**Owen**, T. C. A Grignard reagent from *p*-bromodimethylaniline, 465.

P

**Pace**, R. J., **Williams**, J., and **Williams**, R. L. Boron hydride derivatives. Part VII. The characterisation of some decaborane derivatives of the type, $B_{10}H_{12}$,2M, 2196.
**Packer**, J. E. See **Davies**, A. G., 4390.
**Packer**, K. J. See **Harris**, R. K., 4736, and **Massey**, A. G., 5554.
**Paddock**, N. L. See **Chapman**, A. C., 1825, **Craig**, D. P., 1376, and **Hartley**, S. B., 430.
**Pagdin**, B. See **Holt**, G., 4514.
**Paine**, D. H. See **Chapman**, A. C., 1768.
**Palit**, S. R. See **Kalidas**, C., 3998.
**Palmer**, W. G. The preparation and methods of determination of hypophosphate, 1079.
The vibrational spectra and structures of dithionate, hypophosphate, and related ions, 1552.
**Pande**, K. C. See **Eaborn**, C., 297, 3715, 5082.
**Pannell**, J. See **Millen**, D. J., 1322.
**Paoletti**, P. See **Ciampolini**, M., 2994, and **Sacconi**, L., 4250, 5115.
**Parish**, R. V. See **Barclay**, G. A., 4433.
**Parker**, A. C. See **Chapman**, J. H., 2075.
**Parker**, A. J. Solvation of ions. Part II. Dipolar aprotic solvents as media for nucleophilic substitution reactions at a saturated carbon atom. Part III. The $S_N2$ reactivity of some Group VI anions, pyridine, and alkyl halides in dipolar aprotic solvents, 1328, 4398.
**Parker**, J. B., and **Smith**, T. D. The reaction of thiourea with dialkyl phosphites and trialkyl phosphates, 442.
**Parker**, R. See **Jeffery**, G. H., 570.
**Parker**, R. E. See **Addy**, J. K., 1708.
**Parkinson**, A. R. See **Birchall**, J. M., 2204.
**Parkyns**, N. D., and **Ubbelohde**, A. R. Electron-donor and -acceptor complexes with aromatic systems. Part VI. Complexes of nonacyclic aromatic molecules, 2110.
**Parkyns**, N. D. See also **Martin**, G. C., 4958.
**Parnell**, E. W. Reactions of some substituted benzo-1,2,3-triazines, 4930.
**Parnell**, E. W. See also **Berg**, S. S., 5275.
**Parris**, M. See **James**, B. R., 4630.
**Parsons**, J. A. See **Webb**, R. F., 4092.
**Patai**, S., and **Zabicky**, J. Kinetics and mechanism of substitution at the central carbon atom of tri-*p*-nitrophenylmethyl-chloride in glacial and aqueous acetic acid, 5479.
**Patai**, S. See also **Armour**, C., 412.
**Patel**, M. D., **Rowson**, J. M., and **Taylor**, D. A. H. An alkaloid from *Callichilia* species, 2587.
**Patel**, M. G. See **Lele**, S. S., 969.
**Patrick**, C. R. See **Gething**, B., 1574.
**Pausacker**, K. H. See **Dyall**, L. K., 18.
**Pauson**, P. L., and **Williams**, B. J. Cyclopentadienes, fulvenes, and fulvalenes. Part I. A hexaphenylfulvalene. Part II. 1,1′-Dihydro-2,3,5,2′,3′,5′-hexa- and 1,1′-dihydro-2,3,4,5,2′,3′,4′,5′-octa-phenylfulvalenes. Part III. 2,3,4-Triphenylcyclopentadienone and related products, 4153, 4158, 4162.
**Pauson**, P. L. See also **Knox**, G. R., 4610, 4615, 4619, **Munro**, J. D., 3475, 3479, 3484, and **Osgerby**, J. M., 4600, 4604.
**Pavlović**, D. See **Asperger**, S., 2142.
**Peace**, R. See **Crombie**, L., 5445.
**Peach**, M. E., and **Waddington**, T. C. Liquid hydrogen chloride as an ionizing solvent. Part III. Solubilities and reactions of some derivatives of Groups IV, V, and VI, 1238.
**Peacock**, R. D. See **Earnshaw**, A., 3132, and **Edwards**, A. J., 4253.
**Peacocke**, A. R. See **Overend**, W. G., 3487.
**Pearson**, B. D. See **Ward**, E. R., 515.
**Pearson**, M. J. See **Gray**, P., 4006.
**Pearson**, R. G. See **Basolo**, F., 2207.
**Peat**, S., **Turvey**, J. R., and **Doyle**, D. The polysaccharides of baker's yeast. Part V. A further study of the mannan, 3918.
**Peat**, S., **Turvey**, J. R., and **Rees**, D. A. Carbohydrates of the red alga, *Porphyra umbilicalis*, 1590.
**Peat**, S., **Whelan**, W. J., and **Edwards**, T. E. Polysaccharides of baker's yeast. Part IV. Mannan, 29.
**Peat**, S., **Whelan**, W. J., **Turvey**, J. R., and **Morgan**, K. The structure of isolichenin, 623.
**Pelchowicz**, Z. Organic phosphorus compounds. Part I. The reaction of dialkylmethylphosphonates and methylphosphonothionates with inorganic acid chlorides. Part II. Dialkyl phosphorothioites and their reaction with chloral, 238, 241.
**Pelchowicz**, Z., **Brukson**, S., and **Bergmann**, E. D., Organophosphorus compounds. Part III. Reactions of the alkali derivatives of dialkyl phosphites, 4348.
**Pelchowicz**, Z., **Kaluszyner**, A., and **Bentov**, M. *N*-Alkylated 5-fluorotryptamines, 5418.
**Pemberton**, M. W. See **Meakins**, G. D., 4676.
**Penfold**, A. R. See **Birch**, A. J., 2286.
**Penneck**, R. J. See **Baker**, W., 3986.
**Percival**, E. See **Drummond**, D. W., 3908, and **Mackie**, I. M., 3010.
**Perkins**, M. J. See **Hey**, D. H., 748.
**Perkins**, N. A. See **Bryce-Smith**, D., 2320.
**Perrin**, D. D. Stability constants of some metal complexes of *ortho*-aminophenols, 2244.
**Perry**, G. S. See **Barrer**, R. M., 842, 850.
**Peters**, D. Simple derivatives of cyclopentadiene. Part III. The adducts of methyl cyclopentadienecarboxylate and cyclopentadiene. Part IV. The dimerisation of methyl cyclopentadiene-1-carboxylate, 1037, 1042.
**Petrow**, V. See **Cooley**, G., 4108, **Ellis**, B., 4111, **Hollingsworth**, B. L., 3664, 3771, and **Kirk**, D. N., 2091, 2821.
**Petryka**, Z. See **Gray**, C. H., 2264.
**Phillipps**, G. H. See **Elks**, J., 4573.
**Phillips**, G. O., and **Criddle**, W. J. Radiation chemistry of carbohydrates. Part VII. Action of $\gamma$-radiation on aqueous solutions of D-sorbitol in oxygen. Part VIII. Action of $\gamma$-radiation on deaerated solutions of D-sorbitol, 3756, 3763.
**Phillips**, L. The pyrolysis of methyl nitrite, 3082.
**Phillips**, L. See also **Bromberger**, B., 5302.
**Philpott**, P. G. See **Osbond**, J. M., 2779.
**Pierson**, W. G. See **Allen**, M. J., 757, 2081.
**Pinchas**, S., **Samuel**, D., and **Weiss-Broday**, M. The infrared absorption of $^{18}O$-labelled benzamide, 1688.
The infrared absorption of $^{18}O$-labelled benzoic acid, benzoyl chloride, and methyl benzoate, 2382.
The infrared absorption of normal and $^{18}O$-labelled *N*-methylbenzamide, 2666.
The infrared absorption of normal and $^{18}O$-labelled *NN*-dimethylbenzamide, 3063.
**Pinchas**, S. See also **Halmann**, M., 3542.
**Pinder**, A. R. See **Hussey**, C. W. T., 3525.
**Pitman**, M., and **Sadler**, P. W. Quaternary derivatives of 2,2′-pyridil dioxime and of 2,2′-bipyridyls, 759.
**Poë**, A. J., and **Vaidya**, M. S. The relative stabilities of halogeno-complexes. Part II. The bond-strengths, 1023.
The $PtCl_6^{2-}$–$I^-$ and $PtBr_6^{2-}$–$I^-$ replacement reactions, 2981.
**Poesche**, W. H. See **Ward**, E. R., 2825.
**Pope**, G. A. See **Baker**, W., 2965.
**Pope**, M. I. See **Gregg**, S. J., 1252.
**Porter**, G. See **Land**, E. J., 3540.
**Postlethwaite**, J. D. See **Hathaway**, B. J., 3215.
**Potts**, K. T. See **Hart**, G., 4267, and **Liljegren**, D. R., 518.
**Powell**, A. D. G. See **Fielding**, B. C., 4579.
**Powell**, D. B., and **Sheppard**, N. Infrared spectra and the stabilities of chelate metal–ethylenediamine complexes, 1112.
**Powell**, D. B. See also **Newman**, G., 477.
**Powell**, H. M. See **Prout**, C. K., 4177.
**Powell**, J. W. See **Akisanya**, A., 3705.
**Powell**, T. See **McGowan**, J. C., 2160.
**Pradhan**, S. K. See **Barton**, D. H. R., 255.
**Praill**, P. F. G., and **Whitear**, A. L. Pyrylium salts and related compounds. Part I. The reaction between olefins and acylium perchlorates, 3573.

**Pratt**, L. See **Bennett**, M. A., 2037, **Burton**, R., 594, **Green**, M. L. H., 4854, **Hoehn**, H. H., 2738, and **Winkhaus**, G., 3807.
**Pratt**, S. A. J. See **Howell**, T. E. W., 3167.
**Preston**, D. R. See **Baker**, W., 2965, 2971.
**Priddle**, J. E. See **Hough**, L., 581, 3178.
**Pridham**, J. B. See **De Belder**, A. N., 4464.
**Pritchard**, R. A. See **Hall**, L. D., 1537.
**Proctor**, G. R. Azabenzocycloheptenones. Part III. 2,3,4,5-Tetrahydro-5-oxo-1-toluene-*p*-sulphonylbenz[*b*]azepine, 3989.
**Prout**, C. K., and **Powell**, H. M. Hydrazinium(1+) as a ligand, 4177.
**Prue**, J. E. See **King**, E. J., 275.
**Pugh**, A. C. P. See **Bamford**, C. H., 2057.
**Purnell**, J. H., and **Quinn**, C. P. The rôle of surfaces in the pyrolysis of n-butane, 4128.
**Purnell**, J. H. See also **Bohemen**, J., 360, 2630.
**Puskás**, M. See **Bognár**, R., 320.
**Pyszora**, H. See **Aubrey**, D. W., 1931.

**Q**

**Quail**, J. W. See **Bartlett**, N., 3728.
**Queen**, A. See **Brittain**, E. F., 2045.
**Quinn**, C. P. See **Purnell**, J. H., 4128.

**R**

**Raab**, R. E. See **Buckingham**, A. D., 5511.
**Radda**, G. K. See **Norman**, R. O. C., 3030, 3247, 3610.
**Rafla**, F. K. See **El-Kholy**, I. E.-S., 4490.
**Rahman**, S. M. K. See **Giles**, C. H., 1209.
**Ralph**, P. D. See **Norman**, R. O. C., 2221, 3247.
**Ramakrishna**, R. S. See **Irving**, H., 1272, 2118.
**Randell**, D. R. See **Dean**, F. M., 792, 798.
**Randmeir**, Z. See **Bergmann**, E. D., 3452.
**Rao**, P. N., and **Axelrod**, L. R. 2-Hydroxy-œstrogens. Part II. Synthesis of 2,3-dihydroxyœstra-1,3,5(10)-trien-17-one and œstra-1,3,5(10)-triene-2,3,16α,17β-tetraol, 4769.
**Raphael**, R. A. See **Kennedy**, J., 3813, 4945, and **Money**, T., 3958.
**Rasburn**, J. W. See **Baddeley**, G., 3828, 3835, 3838.
**Rathbone**, P. See **Gray**, P., 2620, 4006.
**Ravens**, D. A. S. See **McIntyre**, J. E., 4082.
**Rawlinson**, D. J. See **Bell**, R. P., 63, 726.
**Ray**, N. H. See **Case**, J. R., 2066, 2070.
**Ray**, S. K., and **Shaw**, R. A. Phosphorus–nitrogen compounds. Part I. Alkylamino- and dialkylamino-derivatives of cyclotriphosphazatriene, 872.
**Read**, G. See **Gardner**, J. N., 1532, **King**, F. E., 960, and **King**, T. J., 5090.
**Redfern**, J. P., and **Salmon**, J. E. Chromium phosphates. Part II. Phase diagram at 70° and further ion-exchange studies in the system chromium(III)–phosphoric acid, 291.
**Redfern**, J. P. See also **Lucaszewski**, G. M., 39.
**Rees**, C. W. See **Brown**, D. N., 3873, **Deavin**, A., 4979, and **Hey**, D. H., 232.
**Rees**, D. A. Estimation of the relative amounts of isomeric sulphate esters in some sulphated polysaccharides, 5168.
**Rees**, D. A. See **also Peat**, S., 1590.
**Rees**, D. I., and **Stephen**, W. I. Substituted benzidines and related compounds as reagents in analytical chemistry. Part XVII. The *NNN'N'*-tetracarboxymethyl derivatives of some 3,3'-disubstituted benzidines, 5101.
**Reich**, F. See **Albert**, A., 127.
**Reid**, D. H. See **Kirby**, E. C., 163, 1724, 3579.
**Reid**, J. A. W. See **Henbest**, H. B., 5239.
**Reusch**, W. H. See **Autrey**, R. L., 3313.
**Reynolds**, J. J. See **Battersby**, A. R., 524.
**Rhind-Tutt**, A. J. See **Banks**, B. E. C., 3240.
**Riad**, Y. See **Hanna**, S. B., 217, and **Iskander**, Y., 223, 2397, 2402.
**Richards**, G. N. See **Machell**, G., 3308.
**Richardson**, A. C. See **Hough**, L., 5561.
**Richmond**, K. W. See **Fielding**, B. C., 4579.
**Richtmyer**, N. K. See **Buck**, K. W., 3633.
**Rickards**, R. W. See **Birch**, A. J., 889.
**Ridd**, J. H. See **Choguill**, H. S., 822.
**Riley**, B. J. See **Grove**, J. F., 1105.
**Riley**, T. See **Gold**, V., 1676.
**Ritchie**, A. C. See **Attenburrow**, J., 4547.
**Ritchie**, P. D. See **McGee**, J., 1782.
**Roberts**, H. L. See **Case**, J. R., 2066, 2070.
**Robertson**, A. See **Fielding**, B. C., 4579.
**Robertson**, J. M., and **Trotter**, J. Crystal-structure studies of polynuclear hydrocarbons. Part V. 1,2:7,8-Dibenzocoronene. Part VI. 1,12:2,3:4,5:6,7:8,9:10,11-Hexabenzocoronene, 1115, 1280.
**Robertson**, J. M. See also **Arnott**, S., 4183, **Clunie**, J. S., 4382, and **Ferguson**, G., 1976.
**Robertson**, R. E., and **Scott**, J. M. W. The neutral hydrolysis of some allyl and benzyl halides, 1596.
**Robinson**, B., and **Shepherd**, D. M. The preparation of DL-α-methylhistidine dihydrochloride, 5037.
**Robinson**, E. A. The reaction of dichloromethylene with water and with phenoxide ions (Reimer–Tiemann reaction), 1663.
**Robinson**, H. C. See **Clark-Walker**, G. D., 2810.
**Robinson**, P. L. See **Bartlett**, N., 3417, 3549.
**Robinson**, P. S. See **Bagnall**, K. W., 1611, 4060.
**Robinson**, R. A. See **Biggs**, A. I., 388.
**Roger**, R., and **Neilson**, D. G. Studies in stereochemical structure. Part XIV. The resolution of α-hydroxyamidinium chlorides by the use of mandelic acids, 3181.
**Rogers**, H. J. See **Armitage**, R., 1842, and **Haslam**, E., 1829, 1836.
**Rona**, P. See **Loewenthal**, H. J. E., 1429.
**Rosenbaum**, J., and **Symons**, M. C. R. Unstable intermediates. Part XI. Allylic carbonium ions, 1.
**Rosenberger**, M. See **Barton**, D. H. R., 1215.
**Rosene**, C. J. See **Jarboe**, C. H., 2455.
**Rosevear**, D. T. See **Chatt**, J., 5504.
**Ross**, K. M. See **Aspinall**, G. O., 3674.
**Rossotti**, F. J. C. See **Anderson**, D. M. W., 140, 2165, 4201.
**Rothstein**, E. See **Bleazard**, W., 68.
**Roubinek**, L. See **Blakely**, C. F., 1939, **French**, P. V., 1953, and **Murphy**, J., 1964.
**Rowlands**, J. R. The electron spin resonance spectrum of $\cdot CH(CO_2H)\cdot CH_2\cdot CO_2H$ in γ-irradiated DL-aspartic acid hydrochloride, 4264.
**Rowson**, J. M. See **Patel**, M. D., 2587.
**Roy**, D. N. See **Nasipuri**, D., 3361.
**Roy**, S. K. See **Shoppee**, C. W., 1583.
**Rudd**, E. See **Jones**, N., 1342.
**Russell**, D. R., and **Sharp**, D. W. A. The preparation of silver fluoroborate and silver hexafluorophosphate, 4689.
**Russell**, R. C. See **Djerassi**, C., 1448.
**Russell**, R. U., **Salmon**, J. E., and **Tiekze**, H. R. Condensed ions in aqueous solutions. Part II. Compounds of quinquevalent vanadium with orthophosphate, 3211.
**Rydon**, H. N. See **Hall**, A. N., 4290, **Jarvis**, D., 1752, and **Large**, D. G., 1749.

**S**

**Sacconi**, L., and **Paoletti**, P. The co-ordinative power of uranyl. Part IV. The heats of solvation of the bis(dibenzoylmethanato)uranyl complex, 4250.
**Sacconi**, L., **Paoletti**, P., and **Ciampolini**, M. Thermochemical studies. Part VI. Heats and entropies of reaction of transition-metal ions with triethylenetetramine, 5115.
**Sacconi**, L. See also **Ciampolini**, M., 2994.
**Sadler**, P. W. Synthesis of antiviral agents. Part I. Heterocyclic compounds related to isatin 3-thiosemicarbazone, 243.
Hydrogen bonding in some thiosemicarbazones and thioamides, 957.
Spectroscopic studies of quaternary aldoximes and ketoximes, 2162.
**Sadler**, P. W. See also **Pitman**, M., 759.
**Saint-Ruf**, G. See **Buu-Hoï**, N. P., 2258.
**Sakla**, A. B. See **Tadros**, W., 2687.
**Salama**, A. See **Hanna**, S. B., 221.

**Salmon, J. E.** See **Daniel, S. S.**, 86, **Lucaszewski, G. M.**, 39, **Redfern, J. P.**, 291, and **Russell, R. U.**, 3211.
**Salt, C.** See **Clifford, B.**, 3516.
**Samuel, D.**, and **Silver, B.** The existence of the $P^1P^1$-diethyl pyrophosphate ion, 4321.
**Samuel, D.** See also **Halmann, M.**, 3158, and **Pinchas, S.**, 1688, 2382, 2666, 3063.
**Samuel, E.** See **Holan, G.**, 4660.
**Sanchez, M. B.** See **Bowers, A.**, 1859.
**Sanderson, W. A.** See **Cadogan, J. I. G.**, 3879, 5236.
**Sargeant, K.** See **O'Kelly, J.**, 484.
**Sasse, J. M.** See **Badger, G. M.**, 746.
**Sasse, W. H. F.**, and **Whittle, C. P.** Synthetical applications of activated metal catalysts. Part XII. The preparation of symmetrically substituted 2,2′-bipyridyls, 1347.
**Satchell, D. P. N.** Co-catalysis. Part II. The relative efficiencies of halogenated acetic acids as Friedel–Crafts co-catalysts. Part III. A comparison of aliphatic and aromatic carboxylic acids as Friedel–Crafts co-catalysts for stannic chloride, 1453, 3822.
Acylation. Part II. Friedel–Crafts acylation, with stannic chloride as catalyst, in solvents of low dielectric constant, 5404.
**Saunders, F. C.** See **Hey, D. H.**, 554.
**Savage, C. A.** See **Brewster, J. A.**, 3699.
**Saville, B.** The concerted action of fluoride and silver ions on diethyl ethylphosphonothiolate in aqueous solution, 4624.
**Saville, B.** See also **Milligan, B.**, 4850.
**Savory, J.** See **Chambers, R. D.**, 3779.
**Saxton, J. E.** See **Bain, B. M.**, 5216.
**Sayigh, A. A.**, and **Ulrich, H.** Tris-(2-hydroxyethyl) isocyanurate, 3148.
**Sayo, H.** See **Masui, M.**, 4773, 5325.
**Scargill, D.** Deformation frequencies of OH groups in nitrosylruthenium complexes, 4444.
**Scargill, D.** See also **Fletcher, J. M.**, 1705, 2000, and **Hardy, C. J.**, 90, 174, 2658.
**Schoental, R.** See **Mattocks, A. R.**, 5400.
**Schofield, J. A.**, and **Todd, Sir A.** Nucleotides. Part XLVI. A new method for the preparation of nucleoside phosphites, 2316.
**Schofield, J. A.** See also **Jarvis, D.**, 1752, and **Large, D. G.**, 1749.
**Schofield, K.** See **Essery, J. M.**, 3939, and **Mills, B.**, 5558.
**Scott, A. I.** See **Davidson, T. A.**, 4075, **Day, A. C.**, 4067, and **Money, T.**, 3958.
**Scott, J. M. W.** See **Robertson, R. E.**, 1596.
**Scott, P. M.** See **Cromartie, R. I. T.**, 3548.
**Scott, W. P.** See **Cooley, G.**, 4108.
**Searle, G. H.** and **Wilkins, C. J.** Silicon esters of picolinic acid, 3897.
**Searle, H. T.** See **Chapman, A. C.**, 1768, 1825, and **Hartley, S. B.**, 430.
**Searle, T.** See **Armitage, R.**, 1842, and **Haslam, E.**, 1836.
**See, L. B.** See **Beckwith, A. L. J.**, 1304.
**Seelye, R. N.** See **Briggs, L. H.**, 642.
**Segovia, R.** See **Barton, D. H. R.**, 2027.
**Selman, L. H.** See **Armour, C.**, 412.
**Seshadri, T. R.** See **Ganguly, A. K.**, 2787.
**Sethna, S.** See **Lele, S. S.**, 969, **Shah, M. V.**, 2663, and **Shah, N. H.**, 4682.
**Shah, M. V.**, and **Sethna, S.** Chromones and flavones. Part III. Synthesis of some cyano-chromones and -flavones, 2663.
**Shah, N. H.**, and **Sethna, S.** Hydroxyanthracene series. Part IV. Synthesis of some anthraquinone derivatives, 4682.
**Shahak, I.** A simple synthesis of $\alpha\beta$-dialkylacrylic acids, 3160.
**Shahak, I.** See also **Bergmann, E. D.**, 3448, 4033.
**Sharp, D. W. A.** See **Kemmitt, R. D. W.**, 2496, and **Russell, D. R.**, 4689.
**Sharpe, A. G.** See **Miller, J. R.**, 2594.
**Sharpe, A. N.**, and **Walker, S.** Molecular interaction: molecular polarisation of amines in benzene and carbon tetrachloride, 2974.
Electric dipole moments of substituted pyridines, pyridine 1-oxides, and nitrobenzenes, 4522.
**Shaw, B. L.** See **Basolo, F.**, 2207, and **Chatt, J.**, 285.
**Shaw, G.** See **Dewar, J. H.**, 3254, and **Naylor, R. N.**, 4845.
**Shaw, R. A.** See **Ray, S. K.**, 872.
**Sheft, I.** See **Banks, B. E. C.**, 3240.
**Shehab, A. H.** See **El-Assal, L. S.**, 1658.
**Sheldon, J. C.** Molybdenum(II) complexes containing triphenyl-phosphine oxide or -arsine oxide, 750.
**Sheldrick, B.** Crystallographic examination of the α- and β-anomers of D-galactose, 3157.
**Shepherd, D. M.** See **Robinson, B.**, 5037.
**Sheppard, N.** See **Bick, I. R. C.**, 1896, **Birch, A. J.**, 2286, and **Powell, D. B.**, 1112.
**Sherif, S.** See **Baddar, F. G.**, 707.
**Shillaker, B.** See **Brittain, E. F.**, 2045.
**Shoppee, C. W.**, **Craig, J. C.**, and **Lack, R. E.** Acetylenic compounds related to stilbœstrol. Part III. Acetylenic alcohols derived from α-alkyldeoxyanisoins, and the α-alkyl-β-ethynylstilbenes. Part IV. The preparation of α-alkyl-β-ethynyl-4,4′-dihydroxystilbenes, 1311, 2291.
**Shoppee, C. W.**, and **Johnston, G. A. R.** Steroids and Walden inversion. Part LXVIII. The solvolysis of some 3-epimeric 4,4-dimethyl-steroid toluene-*p*-sulphonates, 3261.
**Shoppee, C. W.**, and **Krueger, G.** Aza-steroids. Part II. 3-Aza- and 4-aza-A-homo-5α- and -5β-androstane, and the structure of neosaman, 3641.
**Shoppee, C. W.**, and **Lack, R. E.** Steroids and Walden inversion. Part XLIX. Further observations on the bromination of 5α-cholestan-4-one, 3271.
**Shoppee, C. W.**, **Roy, S. K.**, and **Goodrich, B. S.** Steroids and Walden inversion. Part XLVII. 5α-Cholestan-1-one, A-nor-5α-cholestan-1-one, and some derivatives thereof, 1583.
**Short, E. L.** See **Morris, D. F. C.**, 5148.
**Shorter, J.** See **Chapman, N. B.**, 2543, and **Mather, J. G.**, 4744.
**Shoukry, E. M. A.** See **Birch, A. J.**, 5376.
**Shrivastava, H. N.**, and **Speakman, J. C.** The crystal structures of the acid salts of some monobasic acids. Part V. Rubidium hydrogen di-*o*-nitrobenzoate and potassium hydrogen di-*p*-nitrobenzoate, 1151.
**Siddalingaiah, K. S.** See **Büchi, G.**, 2843, and **Crombie, L.**, 2876.
**Siddiqi, I. R.** See **Foster, A. G.**, 4906.
**Silver, B.** See **Samuel, D.**, 4321.
**Silver, H. B.** See **Biddulph, R. H.**, 1822.
**Sim, G. A.** See **Arnott, S.**, 4183, and **Ferguson, G.**, 1976.
**Simpson, W. B.** See **Donaldson, J. D.**, 839.
**Singh, A. P.** See **Frazer, M. J.**, 4680.
**Siragusa, J. A.** See **Allen, M. J.**, 757, 2081.
**Skidmore, S.**, and **Tidd, E.** The quinoline series. Part II. The reaction between quinaldine and sulphuric acid, 1098.
**Skinner, H. A.** See **Bennett, J. E.**, 2472.
**Slater, G. P.** See **Henbest, H. B.**, 4472.
**Slater, N. B.** Theoretical temperature-dependence of the rate of isomerization of cyclopropane, 606.
**Slaytor, M.** Se **Birch, A. J.**, 4692.
**Sly, J. C. P.** See **Carrington, T. R.**, 4560, and **Dibbo, A.**, 2890.
**Smith, A. C. B.** See **Harrison, D.**, 4827.
**Smith, D.** See **Giles, C. H.**, 1209.
**Smith, D. R.** See **Chapman, A. C.**, 1768.
**Smith, E. B.** See **Spice, J. E.**, 3021.
**Smith, E. M.** See **Norman, R. O. C.**, 3247.
**Smith, F.**, and **Stephen, A. M.** *Virgilia oroboides* gum. Part II. Isolation of oligosaccharides after partial hydrolysis, 4892.
**Smith, G. F.**, and **Walters, A. E.** Indoles. Part V. 3-Alkylindole dimers, 940.
**Smith, G. F.** See also **Edwards, P. N.**, 152, 1458.
**Smith, G. H.** See **Knox, G. R.**, 4619.
**Smith, H.** See **Birch, A. J.**, 3128.
**Smith, J.**, and **Thomson, R. H.** Naturally occurring quinones. Part V. Spinochromes E and N, 1008.
**Smith, J. B.** See **Overend, W. G.**, 3487.
**Smith, J. K.** See **Lappert, M. F.**, 3224.
**Smith, J. W.** Steric repression of the mesomeric effect in derivatives of *NN*-dimethylaniline. The mesomeric moments of amino-, methylamino-, and dimethylamino-groups, 81.
The dipole moments of some acetylamino-compounds and the preferred conformation of the acetylamino-group, 4700.

XUM

**Smith**, M. See **Kelly**, P., 1479, 1487.
**Smith**, N. H. P. The effect of polyphosphoric acid on the α- and the β-form of 2-bromo-5-nitroacetophenone oxime, 4209.
**Smith**, N. H. P. See also **Baddeley**, G., 2516.
**Smith**, P. W. See **Lewis**, J., 4590.
**Smith**, R. See **Mandleberg**, C. J., 2464.
**Smith**, T. D. The formation of ferrocenium thiocyanate in mixed aqueous solvents, 473.
The chelates formed by tin(II) with certain amino-polycarboxylic acids, 2554.
The reaction of dialkyl phosphites and trialkyl phosphates with sodium *NN*-diethyldithiocarbamate, 3164.
The preparation of ammonium alkyl hydrogen phosphites, 5050.
**Smith**, T. D. See also **Parker**, J. B., 442.
**Smith**, T. J. See **Burdon**, J., 4519.
**Smith**, W. R. D. See **Cresswell**, R. M., 4882.
**Sobell**, M. See **Capon**, B., 5172.
**Sobotka**, M. See **Belcher**, R., 480.
**Sobótka**, W. See **Eckstein**, Z., 1370.
**Soliman**, G. See **El-Kholy**, I. E.-S., 4490.
**Solymosi**, F., and **Szabó**, Z. G. Effect of defect structure on the rate of formation of spinels, 2745.
**Somerfield**, G. A. See **Bokečia**, M. M., 4663.
**Sondheimer**, F., **Klibansky**, Y., **Haddad**, Y. M. Y., **Summers**, G. H. R., and **Klyne**, W. The methylation of 5α-cholest-6-en-3-one: further examples of the boat conformation of ring-A in the steroids, 767.
**Soutter**, R. A., and **Tomlinson**, M. Attempts to prepare 1,2,3,4-tetrahydro-,9,10-diazaphenanthrenes from cyclohexane-1,2-dione monophenylhydrazones, 4256.
**Speake**, R. N. See **Birch**, A. J., 2286.
**Speakman**, J. C., and **Mills**, H. H. The crystal structures of the acid salts of some monobasic acids. Part VI. Sodium hydrogen diacetate, 1164.
**Speakman**, J. C. See also **Shrivastava**, H. N., 1151.
**Spedding**, H. Intramolecular hydrogen bonding in methyl 4,6-*O*-benzylidene-D-aldohexosides, 3617.
**Speed**, J. A. See **Cavell**, E. A. S., 226.
**Sperry**, J. A. See **Eaborn**, C., 4921.
**Spice**, J. E., **Harrow**, G. A., **McGowan**, C. R., and **Smith**, E. B. Solid transitions in mixed crystals of ethylene dichloride and ethylene dibromide, 3021.
**Spilsbury**, J. F., and **Wilkinson**, S. The isolation of festuclavine and two new clavine alkaloids from *Aspergillus fumigatus* Fres, 2085.
**Spinner**, E. See **Albert**, A., 2689, 5267, and **Milligan**, B., 1919.
**Spring**, F. S. See **Currie**, A. C., 4693, and **Laird**, W., 2638.
**Springall**, H. D. See **Law**, H. D., 279.
**Srimany**, S. K. See **Chatterjee**, A., 4576.
**Srivastava**, G. See **Mehrotra**, 4045.
**Stacey**, M. See **Bailey**, A. J., 4086, **Barker**, S. A., 3995, 5256, **Bolton**, C. H., 4831, and **Foster**, A. B., 1204, 4649.
**Stacey**, M. H. See **Irving**, H., 2019.
**Stafford**, S. L. See **Coyle**, T. D., 743, 3103.
**Stafford**, W. H. See **Miller**, W., 4485.
**Stamp**, A. See **Barker**, C. C., 1285, 3445.
**Stansfield**, F. See **Birch**, A. J., 5376.
**Stephen**, A. M. See **Smith**, F., 4892.
**Stephen**, W. I. See **Belcher**, R., 480, and **Rees**, D. I., 5101.
**Stephens**, R. See **Barbour**, A. K., 808.
**Stephenson**, L. See **Bailey**, E. J., 4535, **Dibbo**, A., 2645, 2890, and **Elks**, J., 4531.
**Sternhell**, S. See **Barton**, D. H. R., 255.
**Stevens**, T. S. See **Carter**, P., 1743.
**Stevenson**, R. See **Laird**, W., 2638.
**Stewart**, M. A. A. See **Bagnall**, K. W., 1611, 4060.
**Stimson**, V. R., and **Watson**, E. J. Catalysis by hydrogen halides in the gas phase. Part V. t-Pentyl alcohol and hydrogen chloride, 1392.
**Stirling**, C. J. M. See **Henbest**, H. B., 5239.
**Stone**, F. G. A. See **Coyle**, T. D., 743, 3103.
**Stone**, R. H. See **Maccoll**, A., 2756.
**Stroud**, D. B. E. See **Barker**, S. A., 3995.
**Struck**, R. F. See **Kosolapoff**, G. M., 2423.
**Strumsa**, J., and **Ginsburg**, D. Alicyclic studies. Part XVI. The Diels–Alder reaction of bi(cyclo-oct-1-enyl) with *p*-benzoquinone and steric interconversions of the primary adduct. Part XVII. Preparation and reactions of bicyclodec-1-enyl. Part XVIII. Homologous cyclic lactone-acids, 1505, 1512, 1514.
**Sturgeon**, R. J. See **Aspinall**, G. O., 3667.
**Summers**, G. H. R. 3α,5-Cyclo-6β-methyl-25D-spirostan-6α-ol and 3α,5-cyclo-6α-methyl-25D-spirostan-6β-ol, 1821.
**Summers**, G. H. R. See also **Bancroft**, G., 3295, and **Sondheimer**, F., 767.
**Suschitzky**, H. See **Ariyan**, Z. S., 2242.
**Sutton**, L. E. See **Browning**, M. C., 4816, and **Coussmaker**, C. R. C., 2705.
**Swan**, J. M. See **Milligan**, B., 1194, 1919, 4266, 4850, 5552.
**Swart**, E. R. See **Casapieri**, P., 4342.
**Sykes**, A. G. Evidence for a single-stage two-electron exchange in the thallous–thallic reaction, 5549.
**Sykes**, P. See **Biggs**, J., 2595.
**Symons**, M. C. R. See **Arotsky**, J., 12, **Clark**, H. C., 7, **Grace**, J., 47, **Kläning**, U., 3204, and **Rosenbaum**, J., 1.
**Szabó**, L. See **Szabó**, P., 448.
**Szabó**, P., and **Szabó**, L. Phosphorylated sugars. Part III. The formation of five-, six-, and seven-membered cyclic phosphates of 1,2-*O*-isopropylidene-D-glucofuranose, and the synthesis of two new cyclic phosphates of D-glucose, 448.
**Szabó**, Z. G. See **Solymosi**, F., 2745.
**Szelke**, M. See **Jansen**, A. B. A., 405.

T

**Tadros**, W., and **Aziz**, G. Reactions with asymmetric diarylethylenes. Part VI. Reduction of 2-bromo-1,1-di-*p*-alkoxyphenylethylenes by thiophenols, and addition of these thiols to 1,1-di-*p*-alkoxyphenylethylenes, 2684.
**Tadros**, W., **Sakla**, A. B., and **Helmy**, A. A. A. Reactions with asymmetric diarylethylenes. Part VII. A new synthetic route to tetra-arylallenes, 2687.
**Taha**, M. I. The reaction of 2-amino-2-deoxy-D-glucose hydrochloride with aqueous ammonia, 2468.
**Takagi**, S., and **Uyeo**, S. A synthesis of 1-ethyl-1,2,3,5-tetrahydro-10-methyl-7,8-methylenedioxy-5-oxobenzo[*f*]pyrrocoline, a degradation product of lycorine, 4350.
**Tam**, S. W. See **Arthur**, H. R., 3551.
**Tamari**, M. See **Bergmann**, F., 4468.
**Tate**, J. M. See **Blake**, D., 618, 756.
**Tate**, M. E. See **Angyal**, S. J., 4116, 4122.
**Tatlow**, J. C. See **Barbour**, A. K., 808, **Bourne**, E. J., 1771, **Brooke**, G. M., 802, **Burdon**, J., 4519, **Fuller**, G., 3198, and **Gething**, B., 1574.
**Taylor**, A. F. See **Bayles**, J. W., 417.
**Taylor**, D. A. H. The synthesis of 3-oxototaryl methyl ether, 3319.
**Taylor**, D. A. H. See also **Akisanya**, A., 3705, and **Patel**, M. D., 2587.
**Taylor**, G. R. See **Allison**, J. M., 3353.
**Taylor**, H. See **Chapman**, N. B., 1908.
**Taylor**, H. T. See **Jones**, N., 1342, 1345.
**Taylor**, J. H. See **Eley**, D. D., 3867.
**Taylor**, K. J. See **Gee**, G., 4298.
**Taylor**, N. H. See **Barber**, M., 3323.
**Taylor**, P. J. M. See **Foster**, A. B., 1204.
**Taylor**, R. See **Baker**, R., 4927, and **Eaborn**, C., 247, 1012, 2388.
**Taylor**, W. See **Corbett**, W. M., 5041.
**Taylor**, W. H. See **Miller**, W., 4485.
**Tebby**, J. C. See **Crabtree**, A., 3497, and **Johnson**, A. W., 2126.
**Tedder**, J. M. See **Fredricks**, P. S., 3520, and **Hoop**, G. M., 4685.
**Templeton**, J. F. See **Barton**, D. H. R., 255.
**Tewari**, K. C. See **Krishna**, B., 3097.
**Tewfik**, R. See **Iskander**, Y., 2393, 2402.
**Theobald**, R. S. Carbonic esters of sucrose. Part I. The preparation of *O*-alkyloxycarbonylsucroses. Part II. The polymerisation of *O*-alkyloxycarbonylsucroses. Part III. The direct preparation of poly(sucrose carbonates) from sucrose, 5359, 5365, 5370.
**Thomas**, D. A. See **Ansell**, M. F., 539.
**Thomas**, I. M. See **Barraclough**, C. G., 2601.

**Thomas**, L. F. See **Foster**, A. B., 5005.
**Thomas**, P. J. The thermal decomposition of 1-chloroethyl methyl ether, 136.
**Thompson**, D. T. See **Jackman**, L. M., 4794.
**Thompson**, M. J. See **Beckwith**, A. L. J., 73.
**Thompson**, R. D. See **Hawkins**, E. G. E., 370.
**Thomson**, J. See **Greenwood**, C. T., 1534.
**Thomson**, R. H. See **Lovie**, J. C., 485, and **Smith**, J., 1008.
**Thorpe**, F. G. See **Charman**, H. B., 1121, and **Hughes**, E. D., 1133.
**Tidd**, E. See **Skidmore**, S., 1098.
**Tietze**, H. R. See **Russell**, R. U., 3211.
**Tiley**, P. F. See **Hyne**, R. A., 2348.
**Tilney-Bassett**, J. F. Cyclopentadienylnickel–acetylene complexes, 577.
**Timmis**, G. M. See **Brown**, S. S., 3656, and **Leese**, C. L., 3816, 3818.
**Tittensor**, E. See **Elliott**, K., 2796.
**Tobe**, M. L. See **Baldwin**, M. E., 4637, and **Barraclough**, C. G., 1993.
**Todd**, Sir A. See **Clark**, V. M., 715, 722, and **Schofield**, J. A., 2316.
**Todd**, D. See **Hinton**, R. C., 5454.
**Tomlinson**, M. See **Clifford**, B., 3516, and **Soutter**, R. A., 4256.
**Tomlinson**, R. C. B. See **French**, C. M., 311.
**Tompsett**, A. J. See **Chapman**, N. B., 1291.
**Toms**, B. A. See **Ingram**, G., 117.
**Topsom**, R. D., and **Vaughan**, J. 3-Nitro-2-naphthoic acid, 2253.
**Torrible**, E. G. See **Holmes**, F., 4790.
**Torto**, F. G. An aldobiouronic acid isolated from *Fagara xanthoxyloides* gum, 3166.
The composition of *Afraegle paniculata* mucilage, 5234.
**Tóth**, J. See **Fodor**, G., 3219.
**Toyne**, K. J. See **Chapman**, N. B., 2543.
**Treloar**, F. E. See **Jordan**, D. O., 729, 734, 737.
**Trenholme**, M. W. See **Gee**, G., 4298.
**Trenwith**, A. B. See **Batey**, W., 1388.
**Trippett**, S. The rearrangement of 1-hydroxyalkylphosphines to alkylphosphine oxides, 2813.
**Trippett**, S., and **Walker**, D. M. The phosphobetaines: preparation and properties, 1266.
The use, in Wittig reactions, of phosphonium salts and phosphobetaines containing a basic group, 2130.
**Trippett**, S. See also **Gough**, S. T. D., 4263.
**Tromans**, F. R. See **McGeachin**, H. M., 4777.
**Trotman-Dickenson**, A. F., and **Verbeke**, G. J. O. The pyrolysis of divinylmercury and the strength of the C–H bond in ethylene, 2580.
**Trotman-Dickenson**, A. F. See also **Bercés**, T., 348, 4281, **Falconer**, W. E., 609, 782, 4285, **Fettis**, G. C., 3037, **Grzybowska**, B., 4402, and **Hogg**, W., 1403.
**Trotter**, J. See **Robertson**, J. M., 1115, 1280.
**Trown**, P. W. See **Brown**, B. R., 2478.
**Tsuda**, Y., and **Uyeo**, S. The structure of products derived from tazettine with acetic anhydride and sulphuric acid, 1055.
Stereochemistry of the hemiketal moiety of tazettine, 2485.
**Tsuda**, Y. See also **Masui**, M., 4063.
**Turner**, E. E. See **Bakshi**, S. P., 168, 171.
**Turner**, J. C. See **Battersby**, A. R., 3899.
**Turner**, W. B. Alternaric acid. Part V. Biosynthesis, 522.
**Turner**, W. B. See also **Bu'Lock**, J. D., 1654.
**Turvey**, J. R., **Clancy**, M. J., and **Williams**, T. P. Sulphates of monosaccharides and derivatives. Part II. Periodate oxidation, 1692.
**Turvey**, J. R. See also **Clancy**, M. J., 2935, and **Peat**, S., 623, 1590, 3918.
**Tye**, F. L. Absorption of electrolytes by ion-exchange materials, 4784.
**Tye**, F. L. See also **Jarvis**, J. W., 4483.
**Tyler**, B. J. See **Ashmore**, P. G., 1017.
**Tyrrell**, H. J. V., **Firth**, J. G., and **Kennedy**, M. Optical studies of the Soret effect. Part I. A modified optical beam-displacement method and its application to aqueous silver nitrate solutions, 3432.
**Tyrrell**, H. J. V., and **Wilson**, P. J. Initial thermoelectric power measurements on thermocells with iodine–iodide electrodes at a mean temperature of 30°, 5390.

U

**Ubbelohde**, A. R. See **Martin**, G. C., 4948, 4958, and **Parkyns**, N. D., 2110.
**Ueng**, T. See **Chang**, C. T., 3414.
**Ulbricht**, T. L. V. Sodium iodide in acetic acid as a mild dealkylating agent, 3345.
**Ulrich**, H. See **Sayigh**, A. A., 3148.
**Underhill**, A. E. See **Hathaway**, B. J., 3091.
**Upadhyay**, J. See **Katchalsky**, A., 5198.
**Urbański**, T. See **Eckstein**, Z., 489, 1370.
**Usher**, G. E. See **Bacon**, N., 2255.
**Uyeo**, S. See **Takagi**, S., 4350, and **Tsuda**, Y., 1055, 2485.

V

**Vaghani**, D. D., and **Merchant**, J. R. Reactions of nitriles. Part I. Condensation of methyleneaminoacetonitrile with aldehydes, 1066.
**Vaidya**, M. S. See **Poë**, A. J., 1023, 2981.
**Vandewalle**, M., and **Verzele**, M. The methylation of alkyl 3-alkyl-2,4,6-trihydroxyphenyl ketones and the structure of xanthohumol, 1021.
**Vaughan**, J. See **Fischer**, A., 1093, and **Topsom**, R. D., 2253.
**Venanzi**, L. M. See **Brewster**, J. A., 3699, **Browning**, M. C., 4816, **Coussmaker**, C. R. C., 2705, and **Howell**, T. E. W., 3167.
**Verbeke**, G. J. O. See **Hogg**, W., 1403, and **Trotman-Dickenson**, A. F., 2580.
**Vernengo**, M. J. See **Bick**, I. R. C., 1896.
**Vernon**, C. A. See **Armour**, C., 412, **Banks**, B. E. C., 1698, 3240, 4235, **Barnard**, P. W. C., 2670, and **Bunton**, C. A., 1636.
**Vernon**, J. M. See **Acheson**, R. M., 457.
**Verzele**, M. See **Vandewalle**, M., 1021.
**Vikin**, J. See **Allen**, M. J., 1420.
**Vincze**, I. W. See **Fodor**, G., 3219.
**Voaden**, D. J. See **Hammick**, D. L., 3303.
**Vofsi**, D. See **Asscher**, M., 2261.
**Vogel**, A. I. See **Jeffery**, G. H., 570.
**Volger**, H. C. See **Charman**, H. B., 1142, and **Hughes**, E. D., 1133, 2359.
**Vosper**, A. J. See **Beattie**, I. R., 2106.

W

**Waddington**, T. C. See **Peach**, M. E., 1238.
**Waddington-Feather**, S. See **Ellis**, B., 4111.
**Waight**, E. S. See **Bacon**, N., 2255.
**Walker**, D. M. See **Trippett**, S., 1266, 2130.
**Walker**, J. See **Dean**, B. M., 3394, and **Mijović**, M. P. V., 3381.
**Walker**, P. G. See **Greig**, C. G., 879.
**Walker**, S. See **Sharpe**, A. N., 2974, 4522.
**Walker**, T. See **Dibbo**, A., 2645, 2890.
**Walls**, L. P. See **Barrett**, P. A., 2404.
**Wallwork**, S. C. Molecular complexes exhibiting polarization bonding. Part III. A structural survey of some aromatic complexes, 494.
**Wallwork**, S. C. See also **Eley**, D. D., 3867.
**Walters**, A. E. See **Smith**, G. F., 940.
**Walton**, A. See **Addison**, W. E., 4741.
**Warburton**, W. K. The synthesis of thyroxine and related compounds. Part XVI. The preparation of 3,5-dichloro-D-thyronine: an unexpected Walden inversion, 2651.
**Warburton**, W. K. See also **Dibbo**, A., 2645, 2890.
**Ward**, E. R., and **Johnson**, C. D. Polynitronaphthalenes. Part III. A quantitative study of the further nitration of the ten dinitronaphthalenes, 4314.
**Ward**, E. R., and **Pearson**, B. D. Diaryls. Part III. Reactions of some dihalogenonaphthalenes with lithium amalgam, and simple syntheses of 2,3:6,7-dibenzobiphenylene, 515.
**Ward**, E. R., and **Poessche**, W. H. A quantitative study of the nitration of benzothiazole, 2825.
**Ward**, E. R., and **Wells**, P. R. Nitration of the *N*-acyl-nitronaphthylamines, 4859.
The bromination of the nitronaphthylamines and their *N*-acyl derivatives, 4866.

**Warren,** C. K. See **Barber,** M. S., 4019.
**Warren,** F. L. See **Goosen,** A., 4038.
**Warren,** K. D. The preparation of some 2-substituted 9-diazofluorenes, 1412.
Kinetic studies of the fluorene series. Part I. The acid-catalysed solvolysis of 9-diazofluorene, 2561.
**Washbourn,** K. See **Barber,** H. J., 2828.
**Wassermann,** A. See **Blakely,** C. F., 1939, 1946, **Buchner,** P., 3974, **French,** P. V., 1953, **Katchalsky,** A., 5198, and **Murphy,** J., 1964.
**Waters,** J. A. See **Eaborn,** C., 542.
**Waters,** W. A. See **Cowley,** B. R., 1228, **Jones,** J. R., 630, 4757, and **Marshall,** B. A., 1579.
**Watson,** D. G. See **Arnott,** S., 4183.
**Watson,** E. J. See **Stimson,** V. R., 1392.
**Watson,** H. R. See **Chatt,** J., 2332, 4980.
**Watterson,** K. F. See **Hoehn,** H. H., 2738.
**Watts,** M. L. See **Baker,** W., 3986.
**Watts,** W. E. See **Knox,** G. R., 4619.
**Way,** J. K. See **Campbell,** I. G. M., 2133.
**Weale,** K. E. See **Harris,** A. P., 146.
**Webb,** R. F., **Duke,** A. J., and **Parsons,** J. A. α-Allylated acetaldehydes, 4092.
**Webb,** R. F. See also **Hinton,** I. G., 5051.
**Webber,** J. M. See **Bolton,** C. H., 4831, and **Foster,** A. B., 1204, 5095.
**Webster,** M. See **Beattie,** I. R., 1730.
**Weedon,** B. C. L. See **Barber,** M. S., 1625, 4019.
**Weigel,** H. See **Bourne,** E. J., 35, 1088, and **Hutson,** D. H., 1546.
**Weiss,** J. J. See **Hayon,** E., 3962, 3970.
**Weiss-Broday,** M. See **Pinchas,** S., 1688, 2382, 2666, 3063.
**Welch,** J. H., and **Gutt,** W. High-temperature studies of the system calcium oxide–phosphorus pentoxide, 4442.
**Welch,** V. A. See **Barnard,** P. W. C., 2670, and **Bunton,** C. A., 1636.
**Wells,** P. R. See **Ward,** E. R., 4859, 4866.
**West,** B. O. See **Deacon,** G. B., 3929, 5127.
**West,** T. S. See **Belcher,** R., 667.
**Whalley,** M. Conjugated macrocycles. Part XXXII. Absorption spectra of tetrazaporphins and phthalocyanines. Formation of pyridine salts, 866.
**Whalley,** W. B. See **Apsimon,** J. W., 752, and **Fielding,** B. C., 4579.
**Wheatley,** P. J. The crystal and molecular structure of 3-methylbenzothiazoline-2-thione, 4379.
An *X*-ray determination of the crystal and molecular structure of perchlorofulvalene, 4936.
The crystal and molecular structure of tetrachloro-1,4-bistriethylstannyloxybenzene, 5027.
**Whelan,** W. J. See **Peat,** S., 29, 623.
**White,** E. N. See **Dean,** R. E., 2773.
**White,** G. R. See **Benn,** M. H., 2365, and **Creighton,** A. M., 2375.
**White,** R. F. M. See **Blakely,** C. F., 1939, **Chapman,** A. C., 1768, **Davies,** A. G., 341, and **Heffernan,** M. L., 1382.
**White,** T. See **King,** H. G. C., 3231, 3234, 3538, 3539.
**Whitear,** A. L. See **Praill,** P. F. G., 3573.
**Whitehead,** M. A. See **Lucken,** E. A. C., 2459.
**Whitehurst,** J. S. See **Baisted,** D. J., 4089.
**Whitham,** G. H. The reaction of α-pinene with lead tetra-acetate, 2232.
**Whitham,** G. H. See also **Cross,** B., 1650.
**Whiting,** D. A. See **Büchi,** G., 2843, and **Crombie,** L., 2876.
**Whiting,** K. D. E. See **Dibbo,** A., 2890.
**Whittaker,** N. See **Openshaw,** H. T., 4939.
**Whittle,** C. P. See **Sasse,** W. H. F., 1347.
**Wibberley,** D. G. See **Bragg,** D. R., 5074, and **Coutts,** R. T., 5058, 5205.
**Wickens,** J. C. See **Osbond,** J. M., 2779.
**Wiles,** L. A. See **Ariyan,** Z. S., 4510.
**Wilkins,** C. J. See **Searle,** G. H., 3897.
**Wilkins,** R. G. See **Brown,** D., 3804, and **Candlin,** J. P., 3625.
**Wilkinson,** G. See **Bennett,** M. A., 1418, 2037, **Burton,** R., 594, **Davison,** A., 3172, **Green,** M. L. H., 4854, **Griffith,** W. P., 775, 2259, **Hoehn,** H. H., 2738, and **Winkhaus,** G., 602, 3807.
**Wilkinson,** P. A. See **Attenburrow,** J., 4547.
**Wilkinson,** R. W., and **Williams,** T. F. The radiolysis of tri-n-alkyl phosphates, 4098.
**Wilkinson,** S. See **Spilsbury,** J. F., 2085.
**Williams,** A. See **Gray,** P., 2620.
**Williams,** A. H. Dihydrochalcones of *Malus* species, 4133.
**Williams,** A. J. See **Le Fèvre,** R. J. W., 1671.
**Williams,** B. J. See **Pauson,** P. L., 4153, 4158, 4162.
**Williams,** G. H. See **Davies,** D. I., 562, 3112, 3116, **Hambling,** J. K., 3108, and **Hey,** D. H., 554, 565, 748.
**Williams,** J. See **Pace,** R. J., 2196.
**Williams,** L. A. The structure of certain polyazaindenes. Part VIII. Tetra-azaindenes derived from the reaction of ethyl β-ethoxy-α-ethoxycarbonylcrotonate with 3-amino-1,2,4-triazoles, 3046.
**Williams,** R. J. P. See **James,** B. R., 2007, 4630.
**Williams,** R. L. See **Pace,** R. J., 2196.
**Williams,** T. F. See **Wilkinson,** R. W., 4098.
**Williams,** T. P. See **Turvey,** J. R., 1692.
**Williamson,** D. M. See **Kirk,** D. N., 2821.
**Williamson,** M. M. See **Head,** F. S. H., 2578.
**Willis,** C. J. See **Barr,** D. A., 1351.
**Willis,** H. A. See **Gerrard,** W., 3153, 4255.
**Wilmshurst,** J. R. See **Davies,** W., 4079.
**Wilson,** D. V. See **Edwards,** R. L., 4995, 5003, and **Naylor,** R. N., 4845.
**Wilson,** P. J. See **Tyrrell,** H. J. V., 5390.
**Winfield,** G. See **Dean,** F. M., 792.
**Winkhaus,** G., **Pratt,** L., and **Wilkinson,** G. π-Cyclohexadienylmanganese tricarbonyl and related compounds, 3807.
**Winkhaus,** G., and **Wilkinson,** G. Some diolefincobalt carbonyl complexes, 602.
**Winter,** G. See **Martin,** R. L., 2947.
**Winters,** D. See **Corbett,** W. M., 4823.
**Wojcicki,** A. See **Addison,** C. C., 4839.
**Wood,** H. C. S. See **Cresswell,** R. M., 476, 4882.
**Wood,** P. M. See **Bokadia,** M. M., 4663.
**Woodbridge,** D. T. See **Barnard,** D., 2922.
**Woodcock,** D. See **Faulkner,** J. K., 5397.
**Woodhead,** J. L., and **Fletcher,** J. M. Spectra of ruthenates and perruthenates, 5039.
**Woodhead,** J. L. See also **Fletcher,** J. M., 1705, 2000.
**Woodhouse,** J. M. See **Brown,** B. R., 2478.
**Woolhouse,** R. A. See **Cullinane,** N. M., 3842.
**Wragg,** W. R. See **Barber,** H. G., 2828, and **Bretherick,** L., 2919.
**Wren,** J. J., and **Lenthen,** P. M. Steric inhibition of hydrogen-bonding in solutions of 4-methyl-2,6-di-t-butylphenol, 2557.
**Wright,** A. See **Archibald,** A. R., 1183, and **Manners,** D. J., 2681.
**Wyatt,** P. A. H. See **Dacre,** B., 2962.
**Wynne-Jones,** W. F. K. See **Dodd,** R. E., 2790, and **Miller,** R. E., 4886.

## Y

**Yardley,** J. P. See **King,** T. J., 4308.
**Yates,** K. C. See **Goosen,** A., 4038.
**Yijima,** C. See **Masui,** M., 4063.
**Young,** D. P. Tautomeric forms of streptomycin, 1337.
**Young,** D. W. See **Money,** T., 3958.

## Z

**Zabicky,** J. The kinetics and mechanism of carbonyl–methylene condensation reactions. Part XI. Stereochemistry of the products. Part XII. The elimination step of the base-catalysed condensation in water, 683, 687.
**Zabicky,** J. See also **Patai,** S., 5479.
**Zeelenberg,** A. P., and **Bickel,** A. F. Slow oxidation of hydrocarbons in the gas phase. Part I. Reactions during the induction period of isobutane oxidation, 4014.
**Zissis,** E. See **Buck,** K. W., 3633.
**Zwierzak,** A. See **Michalski,** J., 4904.

# JOURNAL: INDEX OF SUBJECTS, 1961


## A

*Acacia* species, 4-hydroxypipecolic acid and its stereoisomers from, 189.
*Acacia intertexta*, new leucoanthocyanidin (teracacidin) from, 499.
**Acetaldehydes,** α-allylated, prep., 4092.
**Acetamide** complexes of uranium, neptunium, and plutonium, prep., 1611.
**Acetamides,** substituted 2,4-dichlorophenoxy-, rates of alkaline hydrolysis, 2335.
**Acetanilide,** and nuclear substituted derivatives, dipole moments and preferred conformation of the acetylamino-group, 4700.
**Acetic acid,** alkyl esters, and corresponding lactones, kinetics of hydrolysis, 47.
trichloro-, reaction with cyclopentadiene, rôle of carbonium ions in, 1946.
fluoro-, ethyl ester, methylene reactivity in, 3537.
trifluoro-, studies of. Part XVIII, 1771.
9-methyl-6-oxo-$\Delta^{4(10)}$-1-octalyl-, prep., 4211.
*o*-nitrobenzoyl-, methyl and ethyl esters, base-catalysed condensation products of, 5205.
phenyl-, ionisation constant at 25°, 275.
Sodium hydrogen diacetate, crystal structure, 1164.
**Acetic acids,** *o*- and *p*-chlorophenoxy-, metabolism by *Aspergillus niger*, 5397.
phenyl-, dissociation: influence of pressure on the Hammett reaction constant, 1093.
halogenated, relative efficiencies as Friedel–Crafts co-catalysts, 1453.
**Acetic anhydride,** hydrolysis of. Part VI, 2305. Part VII, catalysis by pyridine and methylpyridines in acetate buffers, 4362.
kinetics of hydrolysis in deuterium oxide solution, 2305.
**Acetimidates,** reaction with acid esters of phosphoric acid, 1805.
**Acetoacetic acid,** γγγ-trifluoro-, ethyl ester, cyanohydrins of, 4519.
**Acetone,** hexafluoro-, thermal decomposition, 1388.
*o*-nitrobenzoyl-, base-catalysed condensation products of, 5205.
**Acetones,** perhalogeno-, photolysis, 3015.
**Acetonitrile,** methyleneamino-, condensation with aldehydes, 1066.
**Acetophenone oxime,** 2-bromo-5-nitro-, α- and β-form of, effect of polyphosphoric acid on, 4209.
**Acetylating agents,** Friedel–Crafts, interaction with decalin. Parts III, IV, 3828, 3835.
**Acetylene–cyclopentadienylnickel complexes,** prep., 577.
**Acetylenes,** complexes with platinum(II). Part I, alkynes, 827.
Polyacetylenes, biosynthesis. Part III, 1654. Part IV, rate of synthesis by Basidiomycete B.841, 3544.
**Acetylenic** acids, long-chain, new prep., 351.
compounds related to stilbœstrol. Parts III, IV, 1311, 2291.
**αβ-Acetylenic acid,** enzymic decarboxylation of an, 1532.
**Acetylenedicarboxylic acid,** dimethyl ester, adducts with triphenylphosphine, 2126.
dimethyl ester, reaction with methyl pyrrole-1-carboxylate, 457.
**Acid,** an αβ-acetylenic, enzymic decarboxylation, 1532.
**Acid–base function** in non-aqueous solution. Part II, 417.
**Acid chlorides,** mechanism of hydrolysis. Part VII, 3748.
**Acids,** acetylenic, long-chain, new prep., 351.
aliphatic and aromatic carboxylic, comparison as Friedel–Crafts co-catalysts for stannic chloride, 3822.
**Acids,** alkenoic, ω-aryl, cyclisation of, 206.
amino-, of the cyclohexane series. Part I, 4372.
structurally related to glutamic acid, deamination by nitrous acid, 3284.
Enzymic resolution of serine, 763.
α-anilino-carboxylic, open-chain, pyrolysis, 1782.
aryl carboxylic, and their esters, infrared spectra, 106.
*N*-carboxy-α-amino-, anhydrides of, initiation step in polymerization. Part I, catalysis by tertiary bases, 4989. Part II, effects related to the structure of amine inhibitors, 4992.
fatty, essential. Parts I, II, 2779, 5270.
α-hydroxy, kinetic resemblance between oxidation of pinacol and its monomethyl ether and, 630.
long-chain, prep. Part II, 4409.
monobasic, crystal structures of acid salts of. Parts V, VI, 1151, 1164.
*cis*-olefinic, pure, attempts to prepare, 351.
polycarboxylic, amino-, chelates formed with tin(II), 2554.
straight-chain monocarboxylic, heats of sublimation, 1048.
tertiary, derivatives of, reactions with aromatic compounds. Part XII, 68.
**Acidity function** ($H_0$), in ethylene glycol and ethylene glycol–water mixtures, 3998.
**Acridine,** 3-hydroxy-9-phenyl-, tautomerism in, 1191.
Benzacridines and other nitrogen-heterocyclic derivatives of *m*-ethylaniline, prep., 4836.
**Acrylic acids,** αβ-dialkyl-, simple prep., 3160.
**Acrylonitrile,** polymerisation of, methyl glycosides as transfer agents in, 3308.
reaction with some isoquinoline derivatives, 4939.
**Actinide tetrachlorides,** acetamide complexes of. Part I, 1611.
**Activation parameters** for $S_N1$ solvolysis in 50% aqueous acetone, 2045.
**Active solids,** production by thermal decomposition. Part XIII, 1252.
**Activity coefficients,** of aqueous solutions of choline chloride at 25°, 3100.
of non-electrolytes in aqueous solutions of sugars, 4906.
**Acylation.** Part II, 5404.
Friedel–Crafts, with stannic chloride as catalyst, in solvents of low dielectric constant, 5404.
intramolecular, 2520.
**Acylium perchlorates,** reaction with olefins, 3573.
**Adenosine-5′ pyrophosphate,** oxidative phosphorylation leading to, 722.
**Adiloline** (an alkaloid from *Adina cordifolia*), 2714.
*Adina cordifolia*, an alkaloid (adiloline) from, 2714.
**Adrenochrome,** formation of melanin from, 52.
**Adsorption,** studies in. Parts XII, XIII, 58, 93.
on inorganic solids, anomalous (endothermic) effects of, 93.
*Afraegle paniculata* mucilage, composition, 5234.
**Akuamma,** alkaloids of. Parts II, IV, 152, 1458. (Part III, *Proc. Chem. Soc.*, 1960, 215.)
**Akuammicine,** structure, 152.
decomposition in methanol, 1458.
**β-Alanine,** α-fluoro-, prep., 4669.
**Alantolactones,** tetrahydro-, from reduction of helenin, interrelation, 4721.
**Alaternin** (a quinone), prep., 485.
*Albizzia zygia* (Macbride), gum exudate of, structural studies, 3908.
**Albumin** of egg, synthetic studies relating to the carbohydrate–protein linkage, 4872.

**Alcohols,** acetylenic, prep. from α-alkyldeoxyanisoins and the α-alkyl-β-ethynylstilbenes, 1311.
aliphatic nitro-, infrared absorption. Part I, 1370.
monohydric nitro-, and their chloro- and bromo-derivatives, infrared spectra, 1370.
sugar, prep. of αω-di-*O*-methanesulphonyl derivatives, 3656.
**Aldobiuronic acid** isolated from *Fagara xanthoxyloides* gum, 3166.
**D-Aldohexosides,** methyl 4,6-*O*-benzylidene-, intramolecular hydrogen bonding in, 3617.
**Aldoximes,** quaternary, spectroscopic studies, 2162.
**Aldrin–isodrin series,** cyclisations and rearrangements in, 4809.
**Alga** (*Nitella translucens*), starch-type polysaccharide from, 2914.
red (*Porphyra umbilicalis*), carbohydrates of, 1590.
**Alginates,** counter-ion fixation in, 5198.
of sodium, potassium, and magnesium, influence of counter-ion fixation on molecular weight and shape, 3975.
**Alicyclic studies.** Parts XV—XVIII, 1498, 1505, 1512, 1514.
**Aliphatic compounds,** free-radical substitution in. Part III, 3520.
**Alkaloids,** of akuamma. Parts II, IV, 152, 1458. (Part III, *Proc. Chem. Soc.*, 1960, 215.)
of the Amaryllidaceae. Part IX, 4038.
aporphine, structural correlations in nuclear magnetic resonance spectra with bisbenzylisoquinoline alkaloids, 1896.
bisbenzylisoquinoline. See previous entry.
from *Callichilia* species, 2587.
from *Solanum*. Part XV, 4645.
of ipecacuanha. Part VII, 3899.
tropane, stereochemistry. Parts XIII, XIV, 3219, 3222.
Adifoline, from *Adina cordifolia*, 2714.
Clavine, from *Aspergillus fumigatus* Fres., 2085.
Graveoline, from *Ruta graveolens*, prep., 4360.
Indicine, from *Heliotropium indicum* L., 5400.
Supinine, from seeds of *Trichodesma zeylanicum*, R.Br., 484.
**Alkanes,** lower, and cyclopropane, rates of oxidation of binary mixtures containing, 782.
**Alkoxy-radicals.** Part I, 1788.
**Alkoxyl radicals,** alicyclic, in thermal decomposition of cyclohexyl and 1-methylcyclohexyl nitrite, 2620.
**Alkyl halides,** reactions with carbene, 1495.
**Alkynes,** complexes with platinum(II), 827.
**Allenes,** tetra-aryl-, new synthetic route to, 2687.
**Allose:** 3-Acetamido-3-deoxy-D-allose diethyl dithioacetal, prep. and its oxidation by peroxypropionic acid, 1643.
**Allyl halides,** kinetics of neutral hydrolysis, 1596.
**Allylbenzene,** di- and tri-acetylation of, 3564.
**Allylic** carbonium ions, 1.
**Alternaric acid.** Part V, biosynthesis, 522.
**D-Altrose,** 3-acetamido-3-deoxy-, derivatives of, prep. and conversion into 2-acetamido-2-deoxy-D-ribose, 1463.
**L-Altrose,** 6-deoxy-2,5-di-*O*-methyl-, conversion of 2,5-di-*O*-methyl-L-rhamnose into, 4649.
**Alumina,** chromatographic, mechanism of adsorption of aromatic hydrocarbons by, 58.
**Aluminium,** tropylium complex halide salts of, 2320.
chloride, action on some *o*-alkylbenzenesulphonic acids and *o*-alkyldiphenyl sulphones, 4514.
$Al_2Br_4.C_7H_8$ complex, crystal structure, 3867.
**Amaryllidaceae,** alkaloids of. Part IX, 4038.
**Amides,** of the " nitrogen mustard " type, prep., 2365.
thio-, hydrogen bonding in, 957.
thio-, prep. by extensions of the Kindler reaction, 1194.
**Amidines,** chemotherapeutic, search for. Parts XVIII, XIX, 1029, 5097.
4,4′-Diamidinodiphenylamines, substituted, prep., 1029.
**Amidinium chlorides,** α-hydroxy-, resolution by use of mandelic acids, 3181.
**Amination,** direct, of mesitylene by hydrazoic acid in concentrated sulphuric acid, 4685.
**Amines,** characterisation by use of (−)-di-*O*-*p*-toluoyltartaric acid, 4675.
polarisation in benzene and carbon tetrachloride, 2974.
aliphatic, mechanism of reaction with carbon tetrachloride, 2261.
**Amines,** aliphatic, reaction with molybdenum(v) chloride, 24.
*N*-arylglycosyl-, isomeric, prep., 323.
*N*-arylhexosyl- and aryl-, transglycosylation, paper-chromatographic investigation, 320.
4,4′-diamidinodiphenyl-, substituted, prep., 1029.
2-halogenoethyl-, di-*N*-substituted. Parts IV, V, 1076, 1291.
2-halogenoethyl-, *NN*-bis-2′-aryloxyethyl, prep., reactivity, and pharmacology, 1076.
heterocyclic tertiary, double methopicrates, prep., 3845.
2-hydroxyethyl-, *NN*-substituted, stability constants of silver complexes of, 3169.
β-hydroxyphenethyl-, hydramine fission of, 4576.
diphenyl-, substituted 4,4′-diamidino-, prep., 1029.
tertiary, interaction with phosphorus pentachloride, 1730.
Cyclohexylamine, deamination by [$^{18}$O]nitrous acid, 761.
Diethylenetriamine, heats and entropies of reaction with transition-metal ions, 2994.
*N*-Methyldi-(2-chloroethyl)amine, reaction with thiosulphate, 679.
Triethylenetetramine, heats and entropies of reaction with transition-metal ions, 5115.
**Amino-,** methylamino-, and dimethylamino-groups, mesomeric moments of, 81.
**Amino-compounds,** acetyl-, dipole moments, and preferred conformation of the acetylamino-group, 4700.
**Amino-radical,** dimethyl- (·$NMe_2$), reactions, 1228.
**Amino-sugars,** and related compounds. Part VIII, 1204.
**Ammonia,** liquid, glow-discharge electrolysis in, formation of hydrazine by, 5177.
liquid, contact glow-discharge electrolysis of, 5186.
**Ammonium salts,** heterocyclic quaternary, dimethinecyanine salts from 1-formylazulenes and, 163.
**Ammonolysis** of hexahalogenotitanates, 95.
**Amœbicidal activity,** chemical constitution and. Part VI, 4711.
**Amylopectin–iodine complexes,** absorption spectra, 1183.
**Analysis,** organic, submicro-methods. Part XIII, 480.
**5α- and 5β-Androstane,** 3-aza- and 4-aza-A-homo-, prep., 3641.
**5α-Androstan-3-one,** 17β-hydroxy-11β-methyl-, prep., 2091.
17β-hydroxy-11-methylene-, prep., 2091.
**Anhydrides,** of *N*-carboxy-α-amino-acids, initiation step in polymerization of. Part I, catalysis by tertiary bases, 4989. Part II, effects related to the structure of amine inhibitors, 4992.
cyclic, in sulphuric acid, 2191.
perfluoro-carboxylic, reaction with *N*-aroylglycines, 1771.
**Aniline,** competition with phenol for triphenylmethyl cation, 575.
*p*-bromodimethyl-, Grignard reagent from, prep., 465.
*m*-ethyl-, benzacridines and other nitrogen-heterocyclic derivatives of, prep., 4836.
2,5-diethyl-, prep. from Friedel–Crafts reaction on *o*-ethylacetanilide, 384.
*p*-iodo-, mechanism of protodeiodination, 822.
*NN*-dimethyl-, steric repression of the mesomeric effect in derivatives of, 81.
**Anilines,** substituted, heat of ionization, 2572.
substituted, ionisation constants of, 388.
α-Anilino-carboxylic acids, open-chain, pyrolysis, 1782.
Benzanilides, *N*-alkyl-2-amino-2′- and -4′-methoxy-, abnormal reactions of diazonium salts from, 232.
**Anilino-radical,** a stable, 3540.
**Anion-exchange resin,** adsorption of uranyl sulphate from 20% methanol by, 1819.
**Anisoins,** α-alkyldeoxy-, prep. of acetylenic alcohols from, 1311.
**Anisole,** acetylation by acetic acid in presence of boron trichloride, kinetics, 1676.
**Anisoles,** kinetics of bromination of, 63.
3-alkyldihydro-, base-catalysed isomerisation, 5376.
*Anogeissus schimperi* gum, constitution, 3461.
**Anthracene,** reactions with oxygen and thiols, 1304.
hydroxy-, series. Part IV, 4682.
9-methyl- and 9,10-dimethyl-, isomeric amido- and amino-derivatives of, prep. and stereochemistry, 588.
Bi(anthracene-9,10-dimethylene), prep., 3741.
**Anthracenes,** 10,9-borazaro-, prep., 425.
substituted, transmission of polar effects in, 2221.

**Anthraquinone**, some derivatives of, prep., 4682.
4,5,7-trimethoxy-2-propyl-, prep., 4691.
**Antibiotics**, carbohydrate components of. Part I, 4831.
**Antimony** trichloride, solutions of organic chlorides in, conductance data at 75°, 1711.
halides, as solvents. Part II, 1711.
Stibine, conductimetric titration with sodium in liquid ammonia, 2676.
**Antimycin-A complex**, structure, 889.
**Anti-purines**, potential. Part IV, 3818.
**Anti-tumour agents**, potential. Part I, 936.
**Antiviral agents**, prep. Part I, 243.
**Antrycide** (quinapyramine), bisquaternary salts related to, 5275.
**Ants**, black cocktail, insect repellant from, 488.
**Apurinic acids**, alkaline degradation, 1903.
**Aquation**, octahedral, mechanism and steric course. Part IV, 4637.
L-**Arabinitol**, 1,3-*O*-benzylidene-, configuration at the benzylidene acetal carbon atom, 5005.
**Arachidonic acid**, prep., 2779.
**Arenes**, polyfluoro-. Parts III, IV, 2204, 3719.
**Aromatic compounds**, reactions with derivatives of tertiary acids. Part XII, 68.
alkyl-, oxidation in aqueous hydrogen bromide, 4082.
polyfluoro-. Part IX, 1574.
**hydrocarbons**, steric effects on spectra of, 2063.
polynitro-, complex formation in pyridine solutions of, 4886.
**molecules**, nonacyclic, electron-donor and -acceptor complexes with, 2110.
**nucleus**, cumulative effect of substituents on reactions in the side-chain, 4744.
**reactivity**. Parts XII—XXI, 297, 247, 542, 1012, 2388, 3715, 4921, 4927, 5077, 5082.
**systems**, electron-donor and -acceptor complexes with. Parts VII, VIII, 4948, 4958.
transmission of polar effects through. Parts I—III, 2221, 2938, 3247.
**Aromaticity**, studies by nuclear magnetic resonance spectroscopy. Part I, 859.
**Arsenic** analogues of aminodiarylboranes, prep., 1000.
carboxylic acids containing, 1398.
ligands, some new polydentate, 3167.
Arsenates. Part I, 39.
Arsenic acid–chromium(III) system, 39.
Arsine, conductimetric titration with sodium in liquid ammonia, 2676.
Arsine, carboxymethyldichloro-, and related carboxylic acids containing arsenic, 1398.
Arsine, tritertiary, complexes of nickel, palladium, and platinum, 4433.
Arsine, a tetra-tertiary, complexes with transition metals, 4269.
Arsine oxide analogues, complexes of copper(II) with, 2298.
Arsine oxide, triphenyl-, as ligand in tetrahedral complexes of manganese(II), 3735.
Arsinophosphonium salts, prep., 3208.
Diarsines, cyclic. Part VI, 2762.
Diarsonium dihydroxides and dibromides, cyclic quaternary, thermal decomposition, 2762.
Sn–O–As(v) linkages, preparation of monomers and polymers containing, 445.
Triphenylarsine oxide, molybdenum(II) complexes containing, 750.
**Arylation** of benzotrihalides, 554.
DL-**Aspartic acid hydrochloride**, γ-irradiated, electron-spin resonance spectrum of $\cdot CH(CO_2H)\cdot CH_2\cdot CO_2H$ in, 4264.
*Aspergillus fumigatus* Fres., isolation of festuclavine and two new clavine alkaloids from, 2085.
*Aspergillus niger*, metabolism of *o*- and *p*-chlorophenoxyacetic acids by, 5397.
**Asymmetric reactants**, olefinic additions with. Part VI, 670.
**Aucubin** (glucoside of *Aucuba japonica*, Thunb.), 5194.
**Autoprotolysis** of sulphuric acid, heat of, 2962.
**Autoxidation** of ethyl chaulmoograte: course and stereochemistry of homolytic autoxidation, 4390.
**Azabenzocycloheptenones**. Part III, 3989.
**Aza-steroids**. Part II, 3641.
**Azepine**: Benz[*b*]azepine, 2,3,4,5-tetrahydro-5-oxo-1-toluene-*p*-sulphonyl-, prep. and oxidation, 3989.
**Azides**, solutions of, radiation chemistry. Parts I, II, 1479, 1487.
organic, reactions of. Part X, 1408.
**Azine**, *o*-nitroacetophenone, geometrical isomerism in, 5560.
**Azulenes**, condensation with aliphatic aldehydes in the presence of perchloric acid, 3579.
1-formyl-, condensation with heterocyclic quaternary ammonium salts to give dimethincyanine salts, 163.
1-1′Azulenylmethyleneazulenium salts and 1-ethoxymethyleneazulenium salts, prep., 1724.

B

*Bacillus subtilis*, ribitol teichoic acid from the walls of, prep. of 4-*O*-(β-D-glucopyranosyl)-D-ribitol (a degradation product), 2180.
**Baker's yeast**, polysaccharides of. Parts IV, V, 29, 3918.
**Basidiomycete B.841**, rate of polyacetylene synthesis by, 3544.
**Bassic acid** (a triterpenoid), structure, 4308.
**Bentonite**, monomethylammonium, sorption of hydrocarbon mixtures by, 842.
**Benzacridines**, derived from 2,5-diethylaniline, prep., 384.
and other nitrogen-heterocyclic derivatives of *m*-ethylaniline, prep., 4836.
**Benzaldehyde**, pentafluoro-, prep., 808.
**Benzamide**, *N*-methyl-, infrared absorption of normal and $^{18}O$-labelled, 2666.
*NN*-dimethyl-, normal and $^{18}O$-labelled, infrared absorption, 3063.
$^{18}O$-labelled, infrared absorption, 1688.
**Benz[*b*]azepine**, 2,3,4,5-tetrahydro-5-oxo-1-toluene-*p*-sulphonyl-, prep. and oxidation, 3989.
**Benzene**, heat of mixing with carbon tetrachloride, 3425.
hydrogenation over nickel in a flow system, 302.
pyrolysis, 3400.
homologues, heterolytic and homolytic substitution by thiocyanogen chloride, 2428.
monosubstituted derivatives of, substitution patterns of, 3153.
allyl-, di- and tri-acetylation of, 3564.
*p*-bromo-(1,2-epoxyethyl)-, kinetics of reaction with benzylamine, 1708.
t-butyl-, free-radical halogenation of, 2587.
[*o*- and *p*-$^3H_1$]-t-butyl-, relative reactivities in detritiation, 4927.
chloro-, *p*-methylphenylation of, 3108.
tetrachloro-1,4-bistriethylstannyloxy-, crystal and molecular structure, 5027.
[α-$^{14}$C]ethyl-, pyrolysis, 3407.
pentafluoronitro-, reaction with ammonia, 802.
hexafluoro-, prep., 2204.
nitro-, relative rate of phenylation of, redetermination, 565.
nitro-, *p*-methylphenylation of, 3108.
1,3,5-trinitro-, kinetics of complex-formation with diethylamine and other amines in solution at low temperatures, 2171.
**Benzenes**, halogeno-, rates of detritiation, 2388.
iodonitro-, reduction of, 4260.
nitro-, substituted, electric dipole moments of, 4522.
**Benzenesulphenyl chloride**, *o*-nitro-, sulphides formed with ketones, prep. and oxidation, 367.
**Benzenesulphonic acids**, *o*-alkyl-, action of aluminium chloride on, 4514.
*O*-**Benzenesulphonyl-lactims**, reactions with phosphates, 1641.
**Benzidines**, substituted, and related compounds, as reagents in analytical chemistry. Part XVII, 5101.
3,3′-disubstituted, *NNN′N′*-tetracarboxymethyl derivatives, as reagents in analytical chemistry, 5101.
**Benzil**, conformation as solute in benzene or carbon tetrachloride, 4447.
**Benzimidazoles**, simple, infrared spectra, 2343.
**Benzimidazoline**, 2-oxo-, acyl derivatives of, 4827.

**Benzo[*c*]cinnoline,** bromination, and prep. and ultraviolet absorption spectra of reference compounds, 5029.
**Benzo[*c*][$^{15}$N]cinnoline,** prep., 1404.
**Benzocyclobutene,** prep., 2971.
1,2-diphenyl-, attempted prep., 2965.
prep., 2971.
**Benzocyclobutenes.** Parts I, II, 2965, 2971.
**Benzocyclohepten-1-one,** perhydro-, system, synthetic and stereochemical studies, 5345.
**Benzo-1,4-dioxan,** derivatives of. Part V, 2148.
**Benzoic acid,** ionisation constant at 25°, 275.
*o*-2-carboxyethyl-, compounds derived from, 4687.
*o*-nitro-, acid rubidium salt, crystal structure, 1151.
*p*-nitro-, acid potassium salt, crystal structure, 1151.
$^{18}$O-labelled, infrared absorption, 2382.
methyl ester, $^{18}$O-labelled, infrared absorption, 2382.
**Benzoic acids,** dissociation: influence of pressure on the Hammett reaction constant, 1093.
ionisation of, effect of chlorine as substituent in the aromatic nucleus, 4744.
ethyl esters, alkaline hydrolysis, effect of chlorine as substituent in the aromatic nucleus, 4744.
**Benzoin,** oxidation by cupric citrate, kinetics, 1579.
**Benzophenanthridones,** *N*-methyl, independent prep. and formation by internuclear cyclisation, 3873.
**Benzo[*f*]pyrrocoline,** 1-ethyl-1,2,3,5-tetrahydro-10-methyl-7,8-methylenedioxy-5-oxo-, prep., 4350.
**2*H*-Benzo[*a*]quinolizines,** 3-alkyl-1,3,4,6,7,11b-hexahydro-9,10-dimethoxy-, 2-ketones and 2-alcohols derived from, new prep., 4711.
**Benzoquinones,** alkyl-, photodimers of, 4499.
**Benzothiazole,** quantitative study of nitration of, 2825.
**Benzothiazoline-2-thione,** 3-methyl-, crystal and molecular structure, 4379.
**Benzo-1,2,3-triazines,** substituted, reactions of, 4930.
**Benzotrihalides,** arylation of, 554.
**Benzoyl chloride,** $^{18}$O-labelled, infrared absorption, 2382.
**chlorides,** reaction with aniline, effect of chlorine as substituent in the aromatic nucleus, 4744.
**peroxide,** esters formed in the reaction with aromatic solvents, 562.
**Benzoylacetic acid,** *o*-nitro-, methyl and ethyl esters, base-catalysed condensation products of, 5205.
**Benzyl chloride,** 4-nitro-, reaction with alkali, 217.
inhibition of the influence of the nitro-group upon α-proton-extraction from, 221.
**derivatives,** nitration, mechanism, 2938.
**halides,** kinetics of neutral hydrolysis, 1596.
**Benzylamines,** polychloro-, prep., 1414.
**Benzylidene acetal carbon atom,** configuration at, in 4,6-*O*-benzylidene-D-glucose and 1,3-*O*-benzylidene-L-arabinitol, 5005.
**Bergamottin,** prep., 2246.
**Beryllium,** dissolution in aqueous solutions of mineral acids and ammonium fluoride, 2658.
solvent-extraction of, from aqueous solutions of mineral acids, 174.
**Betaines,** phospho-, containing a basic group, use in Wittig reaction, 2130.
phospho-, prep. and properties, 1266.
**Betulin,** dehydrogenation with mercuric acetate, 3353.
**Betulinic acid,** dehydrogenation with mercuric acetate, 3353.
**Biacetyl,** conformation as solute in benzene or carbon tetrachloride, 4447.
two trimers of, structure, 4882.
**Biaryls.** Part III, 515.
*oo'*-diamino-, oxidation to cinnolines and *N*-oxides, 3695.
**Bicyclodec-1-enyl,** prep. and reactions, 1512.
**Bicyclo[2,2,2]octenone,** benzo-homologues, ultraviolet spectra, 1224.
**Bi(cyclo-oct-1-enyl),** Diels–Alder reaction with *p*-benzoquinone, and steric interconversions of the primary adduct, 1505.
**Bicyclopentyl derivative,** novel, kinetics and mechanism of formation, 1946.
**Bicyclopentyl derivatives,** prep. from cyclopentadiene, 1939.
**Biformene** (diterpene hydrocarbon from *Dacrydium biforme*), 2187.
**3,3'-Bi-indenyl,** prep. and reactions, 1498.
**Bile pigments,** chemistry of. Parts II—IV, 2264, 2268, 2276.
spectrophotometric titration of, 2276.
**Bilenes,** formation of porphyrins by cyclisation of, 2418.
**Bilirubin,** prototropy to a verdinoid pigment, 2268.
**Biliverdin,** prep. and spectral properties, 2264.
**Biologically essential substituents,** interaction with carbonyl groups. Parts II, III, 4047, 4051.
**Biosynthesis,** studies in relation to. Part XXIV, 3128.
of phenols. Part III, 2312.
**Biphenyl,** chlorination in acetic acid, products of, 2749.
rates of detritiation of, 1012.
nitration of, *ortho* : *para* ratios in, 3885.
derivatives of, cyclisation to phenanthridines, 3771.
2,4'-diphenyl- (*op'*-quaterphenyl), prep., 748.
2,2'-Di-t-butylbiphenylcarboxylic acids and 2'-t-butylbiphenyl-2-carboxylic acid, optical studies of, 611.
**Biphenylene,** π-complexes of, 2332.
substituted, formation by an Ullmann reaction, 4261.
2,3:6,7-Dibenzobiphenylene, simple preps. of, 515.
**Biphenylenes.** Part V, 3986.
di- and tetra-methoxy-, prep., 3986.
**2,2'-Bipyridyl,** complex-forming agents similar to. Part I, 4790.
**2,2'-Bipyridyls,** symmetrically substituted, prep., 1347.
**Bixins,** stereochemistry, from nuclear magnetic resonance, 1625.
**Bond energies** and heats of formation. Part V, 3793.
**Bonds,** carbon–carbon double, activation by cationic catalysts. Part X, 3532.
C–H, strength of, 3037.
**π-Bonds,** between (*a*) silicon, phosphorus, sulphur, or chlorine and (*b*) oxygen or nitrogen, rôle of 3*d*-orbitals in, 5486.
**10,9-Borazaroanthracenes,** prep., 425.
**Borazole,** hexamethyl-, π-molecular complex with tetracyanoethylene, 5060.
**Borazoles,** infrared spectra, 1931.
**Boron,** organic compounds of, chemical and spectroscopic evidence for the occurrence of π-character in C–B bonds in, 3103.
organic compounds of, thermochemistry. Part VI, 2472.
organic compounds of, cyclic. Part V, 1931.
organic derivatives of. Part II, 4045.
tropylium complex halide salts of, 2320.
di-isobutyl-t-butyl-, autoxidation of, relative reactivity of t-butyl and isobutyl group in, 341.
chlorides, reactions with acetone, 1103.
trichloride, interaction with trialkyl phosphates, 4095.
trichloride, interaction with dioxan and 1,3-dioxolan, 5545.
trichloride–phosphoryl chloride complex, structure, 4255.
trifluoride as catalyst for acetylation of anisole by acetic acid, kinetics, 1676.
halides, reactions with sulphoxides, 3224.
hydride derivatives. Part VII, 2196.
Borane, aminoditolyl-, and prep. of diarylborinic acids, 4909.
Boranes, aminodiaryl-, and their phosphorus and arsenic analogues, prep., 1000.
Boranes, phosphino-aryl-, 5053.
Borate complexes of diols and polyols, stereochemistry, 922.
Borates, trialkyl, as solutes, molar Kerr constants, apparent dipole moments, and conformations of, 4140.
Boric esters of 1,2- and 1,3-diols, structure and relative stabilities, 931.
Borines, trimeric dialkylphosphino-, and *B*-halogenated derivatives, prep. and infrared spectra, 1822.
Borinic acids, diaryl-, prep., 4909.
Boronic acids, phenyl-, interaction with hexosides, 2325.
Boronic anhydride, *o*-(4-phenylbuta-1,3-dienyl)phenyl-, prep., 3149.
Decaborane, pyrolysis, 5438.
Decaborane derivatives of type $B_{10}H_{12}$,2M, characterisation of, 2196.
Diborane, heats of reaction with olefins, 2472.
Diboron tetrachloride, reaction with trichloroethylene, isobutene, and *cis*- and *trans*-but-2-ene, 356.

**Boron,** Diboron tetrachloride, reaction with ethylene oxide, 1893.
Diboron tetrachloride, reactions with some nitrogen-containing donor molecules, 3348.
Diboron tetrachloride–olefin compounds. Part III, 356.
Polyborate anions, stereochemistry, 922.
Silver fluoroborate, prep., 4689.
So-called "2-triacetylthiophen" (a boron compound), prep., 746.
Sodium borohydride, reduction of 1,2- and 1,3-diketones with, 910.
**Boron–carbon bonds,** $\pi$-character in, chemical and spectroscopic evidence for, 3103.
**Boroxoles,** infrared spectra, 1931.
**Botogenin,** prep. of 3$\beta$-hydroxypregna-5,9(11),16-trien-20-one from, 1859.
**"Boyd's chloride"** (triphenylmethylphosphonic dichloride), structure, 3542.
**Bromination** of some anisoles and phenols, kinetics, 63.
of ethyl malonate and methyl methanetricarboxylate, kinetics, 726.
of the nitronaphthylamines and their *N*-acyl derivatives, 4866.
**Bromoform,** alkaline hydrolysis and bromination of, kinetics, 1413.
**Buphanitine** (nerbowdine), racemisation during Oppenauer oxidations, 4038.
**Butadiene,** 2-phenyl-, prep. from $\alpha$-methylstyrene, 370.
**Buta-1,3-diene,** reaction of methylene with, 4402.
**s-Butane,** rôle of surfaces in pyrolysis of, 4128.
**Butanes,** 2-halogeno-, halogenation of, 3520.
**Butane-1,3-diol,** 3-methyl-, some reactions of, 3251.
**But-1-ene,** 1,1,3,3-tetraphenyl-, reaction with antimony trichloride and hydrogen chloride in benzene, 3532.
**But-2-ene,** 2-methyl-, two pyrylium salts formed in diacetylation of, 3553.
**Butyl.** See also s-Butyl and t-Butyl.
**s-Butylamine,** mono-, di-, and tri-, equilibria with 2,4-dinitrophenol in aprotic solvents, 417.
**Butyric acid,** $\gamma$-(8-oxo-2-tetralyl)-, attempt to cyclise, 2520.
**Butyric acids,** *N*-substituted $\beta$-amino-, and their esters, stability, 5041.

## C

**Cadmium:** Dichloro(ethylenediamine)cadmium, infrared spectrum and structure, 477.
**Calcium,** oxidation in moist oxygen, kinetics, 884.
hydrogen phosphate precipitated from solutions of calcium nitrate and phosphoric acid, stability, 4914.
oxide–phosphorus pentoxide system, high-temperature studies of, 4442.
*Callichilia* species, an alkaloid from, 2587.
**Calorimeter** for heats of mixing, new, 3425.
**Camphane,** (+)-10-bromo-2-chloro-2-nitroso-, crystal and molecular structure, 1976.
**Camphor,** oxidation by peracids, constitution and stereochemistry of the lactone $C_{10}H_{14}O_4$ formed in, 3366.
**Camphoric anhydride,** Friedel–Crafts reactions in anisole and in benzene, 68.
**Capsanthin,** structure, 4019.
**Capsorubin,** structure, 4019.
**Carbamic acid,** *NN*-diethyldithio-, sodium salt, reaction of dialkyl phosphites and trialkyl phosphates with, 3164.
**Carbanilide,** 3,3′-diamidino-, and its congeners, prep., 5097.
**Carbene,** reactions with alkyl halides, 1495.
**Carbohydrate** components of antibiotics. Part I, 4831.
derivatives containing nitrogen. Part I, 4166.
osotriazole formation, scope and mechanism. Parts V, VI, 2957, 3146.
**Carbohydrates,** ionophoresis of. Part VII, 4649.
polarographic reduction, 3487.
radiation chemistry of. Parts VII, VIII, 3756, 3763.
reactions at position 1 of. Parts I, II, 3487, 5172.
of the red alga *Porphyra umbilicalis*, 1590.
**Carbon atom,** saturated, mechanism of electrophilic substitution at. Parts III—VI, 1121, 1133, 1142, 2359.
**Carbon–boron bonds,** $\pi$-character in, chemical and spectroscopic evidence for, 3103.
**Carbon** tetrachloride, heat of mixing with benzene, 3425.
tetrachloride, mechanism of reaction with aliphatic amines, 2261.
Carbonates, cyclic, physicochemical studies of. Part III, 100.
**Carbonium ions,** allylic, 1.
**Carbonyl compounds,** aromatic, condensation with ethyl 2- and 4-pyridylacetate, 5074.
**groups,** interaction with biologically essential substituents. Parts II, III, 4047, 4051.
**Carbonyl–methylene condensation reactions,** kinetics and mechanism. Part XI, stereochemistry of the products, 683. Part XII, elimination step of the uncatalysed condensation in water, 687.
**Carbonyls,** metal, and their derivatives, solvent shifts in infrared spectra of, 2582.
hexa-, of metals of Group VI, reactions with di- and tri-tertiary phosphines, 4980.
**Carotenoids** and related compounds. Part IX, 4019.
**Casticin,** constituent of *Vitex agnus castus* seeds, 2523.
**Catalysis** with evaporated metal films in a flow system. Part I, 302.
by hydrogen halides in the gas phase. Part V, 1392.
**Catalysts,** activated metal, synthetical applications of. Part XII, 1347.
anionic, catalytic action of. Part I, 4653.
**Catalytic action** of metal alkyl–metal halide complexes. Part I, 1733.
**Catechol,** boron derivatives of, prep., 4045.
**Cathodic reduction,** prep. of mixed pinacols by. Part II, 2081.
prep. of unsymmetrical pinacols by, 757.
*Caulerpa* spp., green seaweeds, polysaccharides from. Part III, 3010.
*Caulerpa filiformis,* water-soluble polysaccharides of, 3010.
**Cells:** System methanol–water–hydrochloric acid at 25°, determination of Washburn numbers in, 5308.
Thermocells with iodine–iodide electrodes, initial thermoelectric power measurements at a mean temperature of 30°, 5390.
**Cellulose** and its derivatives, cross-linking of. Parts II—V, 2926, 2930, 4823, 5041.
acetates, secondary, triphenylmethyl derivatives of, fission by hydrogen bromide, 754.
**Cerium:** Ceric sulphate, oxidation of mandelic, DL-malic, and lactic acid by, kinetics and mechanism, 3097.
**Chalcone** type, heterocyclic compounds of, 2242.
**Chalcones,** dihydro-, of *Malus* species, 4133.
**Characeae,** polysaccharides of. Parts I, IV, 2914, 5333.
**Chaulmoogric acid,** ethyl ester, autoxidation: course and stereochemistry of homolytic autoxidation, 4390.
**Chelates,** metal. Parts I, II, 869, 1257.
**Chelating agents** related to cyclohexane-1,2-diamine-*NNN′N′*-tetra-acetic acid, prep., 667.
**Chemical constitution** and physical properties. Part XXXII, 570.
**Chloramine,** kinetics of reaction with tertiary amines, 4172.
**Chlorination** of monosubstituted benzenes with t-butyl hypochlorite, *ortho* : *para*-ratio in, 3604.
of six monosubstituted benzenes by chlorinium ion, *ortho* : *para* ratio, 3610.
of biphenyl in acetic acid, products in, 2749.
of phenanthrene in acetic acid, kinetics and mechanism, 5285.
**Chlorine** activation by redox-transfer. Part I, 2261.
mechanism of replacement in *cis-* and *trans*-chloronitrobis(ethylenediamine)cobalt(III) ions by thiocyanate in methanol, 2142.
trifluoride, gaseous reaction with methane, 5449.
Chlorides and perchlorates, dissociation constants in aqueous acetone, 1817.
[$^{36}$Cl]Chlorine, prep. from [$^{36}$Cl]hydrochloric acid, 639.
**1-Chloroethyl methyl ether,** thermal decomposition of, 136.
**Chlorpheniramine,** resolution of, 2228.
**Cholesta-1,4-dien-3-one,** Mannich reaction with, 3059.
**5$\alpha$-Cholesta-8,24-dien-3$\alpha$-yl and -3$\beta$-yl toluene-*p*-sulphonates,** 4,4,14$\alpha$-trimethyl-, some reactions, 3295.

**5α- and Δ-Nor-5α-cholestan-1-one** and derivatives of, prep., 1583.
**Cholestan-3-one**, 4,4-dimethyl-, derivatives of, prep., 2725.
**5α-Cholestan-4-one**, bromination of, observations, 3271.
**Cholestan-3β-yl acetate**, 5α,6β-dibromo-, hydroxylation by chromic acid, 3162.
**Cholestenone enol acetate**, 4-substituted steroids derived by rearrangement and reduction of, 2478.
**5α-Cholest-6-en-3-one**, methylation of: examples of boat conformation of ring-A in steroids, 767.
**Cholesterol**, $C_{26}$ hydrocarbon from, structure, 4230.
**Cholesteryl benzoylformate** (phenylglyoxylate), reduction of, 168.
**Choline chloride**, activity coefficients of aqueous solutions at 25°, 3100.
**Chromatography**, ascending paper, distribution of water and butan-1-ol on chromatograms, 3935.
gas, speed of analysis by, 433.
gas, columns, diffusional band spreading in. Part I, elution of unsorbed gases, 360. Part II, the elution of sorbed vapours, 2630.
**Chromium** trioxide, fluorination by selenium tetrafluoride, 3549.
phosphates. Part II, 291.
Chromate ions, monosubstituted, ultraviolet spectra, 3204.
Chromium–phthalocyanine complexes and perpendicular conjugation, 1257.
Chromium(III)–arsenic acid system, 39.
Chromium(III)–phosphoric acid system, phase diagram at 70° and ion-exchange studies in, 291.
Tricarbonyltropyliumchromium salts, "normal" reaction with anions, 3475.
**Chromones** and flavones. Part III, 2663.
cyano-, prep., 2663.
**Chrysene** and three methylchrysenes, convenient prep., 4079.
**Chrysenes**, 12-alkyl-6-amino-, prep., 4911.
12-benzyl-, prep., 4911.
four dimethyl-, prep., 212.
**Cinnoline**, polycyclic derivatives of. Parts VI—IX, 1363, 1404, 3695, 5029.
synthesis, new. Part I, 2828.
Benzo[*c*]cinnoline, bromination, and prep. and ultraviolet absorption spectra of reference compounds, 5029.
Benzo[*c*][$^{15}$N]cinnoline, prep., 1404.
**Cinnolines** and their *N*-oxides, oxidation of *oo'*-diaminobiaryls to, 3695.
polycyclic, and their *N*-oxides, ultraviolet absorption, 1363.
**Cinnoline-3-carboxylic acids**, 4-hydroxy-, substituted, from mesoxalyl chloride phenylhydrazones, 2828.
**Citromycetin**, degradation products of: revised structures, 792; prep. and reactions, 798.
**Clerodin**, constitution, 5061.
**Coal-tar bases**, studies of. Part IX, 5556.
**Cobalt**, cyclopentadienyl derivatives, substituted, 4619.
chloride, spectra in non-aqueous solution, 5105.
phosphates. Part II, 86.
Bis(ethylenediamine)cobalt(III) salts, *cis*- and *trans*-dichloro- and *cis*- and *trans*-chlorohydroxo-, aquation of, 4637.
Chlorocobaltate ion, spectra in non-aqueous solution, 5105.
Chloronitrobis(ethylenediamine)cobalt(III) ions, *cis*- and *trans*-, mechanism of replacement of chlorine by thiocyanate in methanol, 2142.
Cobalt(II), organometallic complexes of, 285.
Cobalt(III) ammine phosphates, phase-diagram studies, 86.
Cobalt(III), complexes with ethylenediaminetetra-acetic acid and (+)-propylenediaminetetra-acetic acid, stereospecific reaction with ethylenediamine or (±)-propylenediamine, 2249.
Cobalt(III) ethylenediamine complexes, infrared spectra. Part II, 471.
Diolefincobalt carbonyl complexes, prep., 602.
Sulphatobis(ethylenediamine)cobalt(III) salts, chelated, prep. and properties, 1993.
Sulphitobis(ethylenediamine)cobalt(III) complexes, prep., 3123.
**Co-catalysis**. Parts II, III, 1453, 3822.
**Codeine**, 14-hydroxynor-, and its derivatives, 4693.
**Colchicine**, disposition of the oxygen functions in, 1421.
series, syntheses in. Parts III, IV, 1421, 1429.
**Complexes**, addition, of metals with aromatic systems, prep. and physical measurements in the solid state, 4958.
aromatic, structural survey of, 494.
binuclear, magnetic properties of, 396.
chelate metal–ethylenediamine, infrared spectra and stabilities, 1112.
of copper, determination of oxidation–reduction potentials, 2007.
electron-donor and -acceptor, with aromatic systems. Parts VI—VIII, 2110, 4948, 4958.
electron-donor and -acceptor, of some tetracyclic aromatic and hetero-aromatic molecules, 4948.
halogeno-, relative stabilities. Part II, bond strengths, 1023.
inorganic, spectra in non-aqueous solvents. Part I, 5105.
metal, chelated, double bonding in, 3683.
of metals with *o*-aminophenols, stability constants, 2244.
of metals with bis-[3-di(carboxymethyl)aminopropyl] ether, computation of stability constants with aid of high-speed digital computer, 2019.
molecular, exhibiting polarization bonding. Part III, 494.
molecular, based on derivatives of 4,4'-dihydroxytriphenylmethane, 393.
square-planar, metal–metal interactions in, 4452.
tetrahedral, of nickel(II), and factors determining their formation. Part II, 2705.
of transition metals with seven-membered ring systems. Parts III, IV, 594, 2037.
**$d^3$-Complexes**, magnetic properties of some, 3138.
**$d^4$-Complexes**, magnetic properties of some, 3132.
**Complex-formation** between a variety of organic solutes in carbon tetrachloride, 5434.
of 1,3,5-trinitrobenzene with diethylamine and other amines in solution at low temperatures, kinetics, 2171.
**Complex-forming agents** similar to 2,2'-bipyridyl. Part I, 4790.
**$C_{15}$ compounds**, reaction with acetic anhydride–sulphuric acid, 3539.
**Computer**, high-speed digital, use for computation of stability constants of metal complexes of bis-[3-di(carboxymethyl)-aminopropyl] ether, 2019.
**Condensation reactions**, carbonyl–methylene, kinetics and mechanism. Part XI, stereochemistry of the products, 683. Part XII, elimination step of the uncatalysed condensation in water, 687.
**Condensations** involving linking of carbon to carbon, of carbon to nitrogen, and of carbon to sulphur, influence of pH on, 5211.
**Conductance** of solutions in which the solvent molecule is "large". Part VII, 311.
measurements for determination of dissociation constants of chlorides and perchlorates in aqueous acetone, 1817.
of ferric and cupric stearates in aliphatic hydrocarbons, 466.
data on solutions of organic chlorides in antimony trichloride at 75°, 1711.
of quaternary ammonium toluene-*p*-sulphonates in triaryl phosphites, 311
**Conductimetric titration** of sodium in liquid ammonia with phosphine, arsine, stibine, and germanes, 2676.
**Conductivities** in liquid hydrogen chloride of derivatives of elements of Groups IV, V, and VI, 1238.
electrical, in ethylene carbonate, 100.
**Conformation** and reactivity. Part III, 2543.
**Controlled-potential electrolysis**. Part VI, 4773.
**Co-ordination compounds** having carboxylic esters as ligands. Part I, stoicheiometry, structure, and stereochemistry, 817.
formed by tetrafluorides of the sulphur sub-group, 3417.
**Copper** complexes, oxidation–reduction potentials of, 2007.
complexes of, spectrophotometric and thermodynamic properties, 4630.
Copper(I), tetrakis(methyl cyanide)-, complexes, prep. and properties, 3215.
Copper(II), complexes with phosphine oxides and arsine oxide analogues, prep., 2298.

**Copper,** Copper(II) formate, anhydrous, crystal structure, 3289.
Cupric salts, oxidations of organic compounds by. Part II, 1579.
Cupric stearate, conductance in aliphatic hydrocarbons, 466.
Monopyridinecopper(II) acetate, crystal structure, 5244.
**Coronene:** 1,2:7,8-Dibenzocoronene, crystal structure, 1115.
1,12:2,3:4,5:6,7:8,9:10,11-Hexabenzocoronene, crystal structure, 1280.
**Cortisone,** hydro-, 9α-fluoro-16β-methyl-, prep., 4560.
**Coumaran-3-ones** and other $C_{15}$ compounds, reaction with acetic anhydride–sulphuric acid, 3539.
2-benzyl-2-hydroxy-, occurrence in Quebracho tannin extract, 3234.
**Coumarin:** Bicoumarinyls, 3,3′- and 8,8′-, prep., 969.
3-*O*-*p*-Coumaroylquinic acid, prep., 5153.
**Coumarins,** 8-phenyl-, prep., 969.
**Counter-ion fixation** in alginates, 5198.
**Crotonic acid,** β-ethoxy-α-ethoxycarbonyl-, ethyl ester, reaction with 1,2,4-triazoles, polyazaindenes derived from, 3046.
**Crotonyl esters,** addition of amines to, 2930.
**Cryoscopic determination of molecular weight** (submicro), 480.
**Cryptopimaric acid,** constitution, 752.
**Crystal Violet,** biphenyl analogues, steric effects in, 3445.
**Cyanamide,** disilyl-, prep. and properties, 4879.
**Cyanides,** alkali, reaction with pyrylium salts, 3566.
**Cyanogen chloride,** reaction with sodium salts of carboxylic acids, 3185.
**Cyclic compounds,** reduced. Parts X—XIII, 201, 206, 2903, 2908.
**Cyclisation,** internuclear. Parts XVI, XVII, 232, 3873.
**Cyclitols.** Parts IX—XI, 4116, 4122, 4718.
**Cyclobutane,** 1,2,3,4-tetraphenyl-, action of *N*-bromosuccinimide on, 479.
**Cyclobutanes,** hexafluoro-, some isomeric, prep., 3198.
**Cyclobutenes,** pentafluoro-, some isomeric, prep., 3198.
Benzocyclobutenes. Parts I, II, 2965, 2971.
**Cyclodecene:** Bicyclodec-1-enyl, prep. and reactions, 1512.
**Cycloheptadiene:** 2,3:2′,3′-Dibenzobi(cyclohepta-2,7-dienyl), prep. and reactions, 1498.
**Cycloheptatriene** complexes of Group VI metals, proton resonance spectra, 2037.
Cycloheptatriene– and tropylium–metal complexes. Parts I—III, 3475, 3479, 3484.
rearrangement to benzene complexes, 3479.
*NN′*-Di(cyclohepta-2,4,6-trienyl)urea [*alias* tropylium isocyanate], prep., 482.
Tropylium complex halide salts of boron, aluminium, iron, titanium, and tin, 2320.
**Cycloheptatrieneiron carbonyl** and related compounds, prep., 594.
**Cycloheptene,** acylation of, 1342.
**Cycloheptenone:**
Azabenzocycloheptenones. Part III, 3989.
Perhydrobenzocyclohepten-1-one system, synthetic and stereochemical studies, 5345.
**π-Cyclohexadienylmanganese tricarbonyl** and related compounds, 3807.
**Cyclohexane** series, amino-acids of. Part I, 4372.
1-methylene-4-t-butyl-, stereochemistry of reaction with t-butyl perbenzoate, 1650.
**Cyclohexanecarboxylates,** 4-t-butyl-, kinetics of acid-catalysed hydrolysis of, 2543.
**Cyclohexane-mono- and -di-carboxylates,** methyl, kinetics of acid-catalysed hydrolysis of, 2543.
**Cyclohexane-1,2-diamine-*NNN′N′*-tetra-acetic acid,** chelating agents related to, prep., 667.
**Cyclohexane-*cis*- and -*trans*-1,2-diol,** ethylidene acetals of, prep., 3622.
**Cyclohexane-1,2-dione monophenylhydrazones,** attempts to prepare 1,2,3,4-tetrahydro-9,10-diazaphenanthrenes from, 4256.
**Cyclohexane-1,3-diones.** Parts V—VII, 1683, 3333, 3340.
**Cyclohexanol,** γ-irradiation of, 4086.
**Cyclohexene,** hydrogenation over nickel in a flow system, 302.
γ-irradiation of, 4086.
**Cyclohexene,** 1-1′-acetoxyvinyl-, Diels–Alder reactions, 2903.
reaction with *p*-benzoquinones containing a methoxycarbonyl group, 2908.
3-vinyl-, pyrolysis, 3403.
**Cyclohex-2-enone,** 2-acetyl-, investigations on synthesis of. Part II, some related experiments, and constitution of the dimeric product ($C_{16}H_{20}O_4$), 3525.
**Cyclohex-2-en-1-one,** 3-methoxy-2, 4-diphenyl-, reaction with acetone cyanohydrin, 3340.
3-methoxy-2,5-diphenyl-, reaction with acetone cyanohydrin, 1683.
**Cyclohexyl thiolsulphate,** sodium 2-oxo-, reactions of, 5552.
and 1-methylcyclohexyl nitrite, alicyclic alkoxyl radicals in the thermal decompositions of, 2620.
**Cyclohexylamine,** deamination by [$^{18}$O]nitrous acid, 761.
**Cyclo-octene,** acylation of, 1342.
Bi(cyclo-oct-1-enyl) Diels–Alder reaction with *p*-benzoquinone, 1505.
**Cyclopentadiene,** conversion into bicyclopentyl derivatives, 1939.
simple derivatives of. Parts III, IV, 1037, 1042.
deeply coloured electrically conducting polymers from, prep. and properties, 1953.
reaction with trichloroacetic acid, rôle of carbonium ions in, 1946.
π-Cyclopentadienyl- and cyclopentadiene-iron carbonyl complexes, 3172.
Cyclopentadienylnickel–acetylene complexes, prep., 577.
3-(Cyclopenta-2,4-dienyl)cyclopentyl trichloroacetate, mechanism of formation of a deeply coloured electrically conducting polymer from, 1964.
Dicyclopentadienyl-tin and -lead, infrared spectra and structure, 547.
Di-π-cyclopentadienyl hydrides of tantalum, molybdenum, and tungsten, prep., 4854.
**Cyclopentadienes,** fulvenes, and fulvalenes. Parts I—III, 4153, 4158, 4162.
**Cyclopentadienecarboxylic acid,** methyl ester, adducts with cyclopentadiene, 1037.
**Cyclopentadiene-1-carboxylic acid,** methyl ester, dimerisation, 1042.
**Cyclopentadienone,** 2,3,4-triphenyl-, and related products, 4162.
**Cyclopentadienyl derivatives,** substituted, of nickel, cobalt, iron, molybdenum, and titanium, 4619.
Cyclopentadienyl–metal compounds, variation of bond type in, 690.
**Cyclopentanecarboxylic acid,** 2-oxo-, ethyl ester, reaction with arylamines. Part I, 4295.
**1*H*-Cyclopenta[*c*]quinolines,** 2,3,4,5-tetrahydro-4-oxo-, prep., 4295.
**Cyclopentene,** from thermal unimolecular isomerisation of vinylcyclopropane, 3547.
**Cyclopropane,** thermal isomerisation of, 609.
rate of isomerization of, temperature-dependence, 606.
and lower alkanes, rates of oxidation of binary mixtures containing, 782.
reaction of methoxyl radicals with, 348.
vinyl-, thermal unimolecular isomerisation to cyclopentene, 3547.
" Cyclopropane platinous chloride ", structure, 738.
**$O^2$,3′-Cyclouridine,** prep., 1410.
**Cysteine,** interaction with a coloured maleimide, 2810.
(±)-*S*-3-Methylbut-2-enylhomocysteine, prep., 4692.
Syntheses of poly-(*S*-alkyl-DL-homocysteines), poly-DL-homocysteine, and poly-DL-homocysteic acid, 463.
**L-Cysteine,** L-cysteinyl-tetraglycyl-, oxidation of, 1749.
L-cysteinyl-pentaglycyl-, prep. and oxidation, 1752.
L-cysteinyl-hexaglycyl-, prep. and oxidation, 1752.
**Cytotoxic compounds.** Parts II, III, 2365, 2375.

## D

**Dammar resin,** acidic constituents of, 646.
**Dealkylation,** mild, by sodium iodide in acetic acid, 3345.
**Deamination** (by nitrous acid) of amino-acids structurally related to glutamic acid, 3284.
of glutamic acid, glutamine, and γ-aminovaleric acid, steric course of lactonisation following, 3278.



XUM

**Decalin**, interaction with Friedel–Crafts acetylating agents. Parts III, IV, 3828, 3835.
interaction with isobutyryl chloride–aluminium chloride, 4303.
interaction with propionyl chloride and aluminium chloride, 4306.
novel derivatives of, prep. from 10β-(1,2-dihydroxyethyl)-*trans*-1β-decalol, 3838.
**Decalin-2,9-diols**, the 10-methyl-, prep., 4478.
***trans*-1β-Decalol**, 10β-(1,2-dihydroxyethyl)-, prep. of novel decalin derivatives from, 3838.
**Dec-2-enoic acid**, *trans*-9-oxo-, prep., 3813.
**Defect structure**, effect on rate of formation of spinels, 2745.
**Dehydrogenation** of substituted 1,2-dihydronaphthalenes by quinones, correlation of donor reactivity with the nature of the substituents, 4794.
**Deoxyribonucleic acids**, nucleotide sequence in. Part V, 1903.
**Depsides** of gallic acid, 1836.
**Desosamine**, degradation by alkali: its absolute configuration at position 5, 4831.
**Detritiation** of halogenobenzenes, rates, 2388.
of diphenyl ether, diphenyl sulphide, dibenzofuran, and dibenzothiophen, rates, 5077.
of [*o*- and *p*-$^3H_1$]-toluene and -t-butylbenzene, relative reactivities, 4927.
aromatic, effect of methyl and t-butyl groups in, 247.
**Diaryls**. Part III, 515.
**1*H*-1,7-Diazaindan-2-one**, 2,3-dihydro-3,3-dimethyl-, prep., 747.
**Diazaindenes** and their quaternary salts. Part II, 584.
**Diazo-reaction**, Meerwein's, arylation of 2-furoic acid in, 2576.
**Diazo-exchange reaction** with nitrogen-15: *p*-nitrophenyldiazonium chloride solution, 1825.
**Diazonium chloride**, *p*-nitrophenyl-, diazo-exchange reaction in solution of, 1825.
**salts** from *N*-alkyl-2-amino-2′- and -4′-methoxybenzanilides, abnormal reactions of, 232.
**2,3:2′,3′-Dibenzobi(cyclohepta-2,7-dienyl)**, prep. and reactions, 1498.
**1,2:7,8-Dibenzocoronene**, crystal structure, 1115.
**Dibenzyl hyponitrite**, thermal decomposition in solution, kinetics, 1788.
**Dielectric polarization** of some imperfect gases, 5511.
**Diketones**, symmetrical 1,2- and 1,3-, reduction with sodium borohydride, and separation of diastereoisomeric 1,2- and 1,3-diols by borate complexes, 910.
**β-Diketones**, enol ethers of, structural requirements for the displacement of the alkoxyl by the cyano-group in, 3333.
**1,5-Diketones**, structure, 674.
**Dimethincyanine salts**, prep. from 1-formylazulenes and heterocyclic quaternary salts, 163.
**Dimethylamino radical** (·$NMe_2$), reactions, 1228.
**Dinaphtho(2′,3′-2,3)(2″,3″-4,5)furan**, prep., 765.
**Diols**, and polyols, borate complexes of, 922.
diastereoisomeric, separation by means of borate complexes, 910.
1,2- and 1,3-, boric esters of, structure and relative stabilities, 931.
**Dioxan**, interaction with boron trichloride, 5545.
Benzo-1,4-dioxan, derivatives of. Part V, 2148.
**1,3-Dioxan**, *trans*-5-hydroxy-2-phenyl-, stereochemistry, 2338.
**1,3-Dioxans**, 5-hydroxy-2-*p*-nitrophenyl-, configuration, 2338.
**1,3-Dioxolan**, interaction with boron trichloride, 5545.
**Dipolar molecules**, reactions with ions, effect of solvent composition on kinetics of. Part III, 226.
**Dipole moments**, studies on polyethylene and polypropylene glycols of low molecular weight, 4729.
electric, of substituted pyridines, pyridine 1-oxides, and nitrobenzenes, 4522.
**Dissociation** of benzoic acids and phenylacetic acids: influence of pressure on the Hammett reaction constant, 1093.
constant, acid, of hydrogen sulphide at high pressure, 4678.
constants of some chlorides and perchlorates in aqueous acetone from conductance measurements, 1817.
constants, first acid, of "sulphurous" and phosphoric acids, effect of pressure on, 1765.
**Diterpene hydrocarbon** (biformene) from *Dacrydium biforme*, 2187.
**Diterpenes**, potential intermediates for synthesis of, 960.
**Diterpenoid bitter principles**. Part III, 5061.
**Diterpenoids**, B-nor-, studies in prep., 1105.
**Dithizone**, reactions with organometallic compounds, 1470.
studies with. Parts VII—IX, 1272, 1470, 2118.
and its analogues, action of halogens on, 1272.
**Dithizones**, mono- and di-*p*-bromo-substituted-, and their metal complexes, absorption spectra, 2118.
**Docosa-4,7,10,13,16-pentaenoic acid**, prep., 2779.
**Double bonds**, isolated, ultraviolet absorption of, 2075.
**Dyes**, studies in light absorption of. Part III, 1209.

## E

**Echinulin**, structure of, some remarks on, 3128.
**Ehrlich–Sachs reaction**, molecular structure of products from, 1631.
**Elaidic acid**, rôle of peroxides in autoxidation of, 4324.
**Electrolysis**, controlled-potential. Parts VI, VII, 4773, 5325.
glow-discharge. Parts IV, V, 5177, 5186.
**Electrolytes**, absorption by ion-exchange materials, 4784.
**Electron-transfer reactions** between oxygen and aromatic hydrocarbons, 905.
**Eliminations**, gas-phase. Part II, 2756.
**Ellagic acid**, naturally occurring trimethyl ether of, 642.
**Emetamine**, structure, 3899.
**(±)-Emetamine**, stereospecific prep., 3899.
**Emetine** and related compounds, prep. Part III, 4939.
**Enol ethers** of β-diketones, displacement of the alkoxyl by the cyano-group in, structural requirements for, 3333.
**Epilimonol** iodoacetate, *X*-ray analysis of, 4183.
**Epilumisterol**, oxidation and reduction, 4676.
**Epoxide** reactions, mechanism. Part III, 1708.
**Epoxides**, polymerization of. Part III, 4298.
**Epoxide–episulphide transformation**, in sugars, 1537.
**Ergosterol**, oxidation of, proof of rear approach in, 1880.
**Ericaceae**, Hong Kong, new triterpene from, 551.
**Erythritol**, di-*O*-benzylidene-, structure, 5011.
**Ester hydrolysis**, tracer studies in. Part IX, 943.
**Esters**, α- and β-amino-, optically active, effect of ketones on, 4047.
carboxylic, as ligands in co-ordination compounds. Part I, 817.
β-(diarylphosphino)propionic, abnormal hydrolysis. Part I, 5454.
hemialdal, infrared spectra, 2525.
**Ethane**, 1,1-dinitro-, polarographic behaviour and controlled-potential electrolysis, 5325.
**Ethanol**, irradiation in the liquid and in the solid state and in the presence of solutes, 3962.
**Ether-fission**, acid-catalysed. Part I, a new mechanism in sulphuric acid, 4963.
**Ether**, bis-[3-di(carboxymethyl)aminopropyl], metal complexes of. Computation of stability constants with aid of high-speed digital computer, 2019.
1-chloroethyl methyl, thermal decomposition of, 136.
methyl phenethyl, nitration of, 3030.
**Ethers**, association with *ortho*-substituted phenols, 4762.
and related compounds, oxidaton of. Part I, 5239.
aromatic, interdependence of molecular conformation and conjugation in. Part IV, 2516.
**Ethoxide**, methoxide, and hydroxide ions, comparison of the nucleophilic reactivity in dioxan, 5259.
**Ethoxyl radicals**, 1-phenyl-, in thermal decomposition of 1-phenylethyl nitrite, 4006.
**Ethyl** radicals, reaction with hydrogen bromide, 3037.
1-phenyl-, cation (in polymerization of styrene), 729.
**Ethylene**, strength of C–H bond in, 2580.
tetracyano-, π-molecular complex with hexamethylborazole, 5060.
*cis*-1,2-difluoro-, nuclear magnetic resonance spectrum, 743.
1,1-diphenyl-, dimerisation in benzene–n-butyl-lithium-titanium tetrachloride–hydrogen chloride systems, 1733.
1,1-diphenyl-, interaction with butyl-lithium, 4653.

**Ethylene,** carbonate, electrical conductivities in, 100.
dichloride and dibromide, solid transitions in mixed crystals of, 3021.
sulphate, tetramethyl-, prep., 2257.
**Ethylenes,** asymmetric diaryl-, reactions with. Parts VI, VII, 2684, 2687.
2-bromo-1,1-di-*p*-alkoxyphenyl-, reduction by thiophenols, 2684.
chlorinated, action of γ-radiation on, 4485.
1,1-di-*p*-alkoxyphenyl-, addition of thiols to, 2684.
**Ethylenediamine,** complexes with cobalt(III), infrared spectra. Part II, 471.
chelate complexes with metals, infrared spectra and stabilities, 1112.
**Ethylenediamines,** *NN*-dialkyl-*N'*-arylalkyl-*N'*-4-quinazolyl (*or* 6-methyl-4-pyrimidyl *or* 4-methyl-2-pyrimidyl)-, of potential pharmacological interest, prep., 1908.
Chelated sulphatobis(ethylenediamine)cobalt(III) salts, prep. and properties, 1993.
*cis*- and *trans*-Chloronitrobis(ethylenediamine)cobalt(III) ions, mechanism of replacement of chlorine by thiocyanate in methanol, 2142.
*cis*- and *trans*-Dichloro- and *cis*- and *trans*-chlorohydroxobis(ethylenediamine)cobalt(III) salts, aquation of, 4637.
(Ethylenediamine)-zinc, -cadmium, and -mercury, dichloro-, infrared spectra, 477.
Sulphitobis(ethylenediamine)cobalt(III) complexes, prep., 3123.
**Ethylenediaminetetra-acetic acid** and (+)-propylenediaminetetra-acetic acid, cobalt(III) complexes with, stereospecific reaction with ethylenediamine or (±)-propylenediamine, 2249.
**Eucalyptus calophylla** Kino, leucopelargonidin from, 2787.
*Eugenia maire* A. Cunn., constituents of. Parts I, II, 642, 4684.
**Evolidine** (cyclic heptapeptide), structure, 279.
**Extraction** of beryllium from aqueous solutions of mineral acids by alkyl esters of phosphoric acid, 174.
of nitric acid from aqueous solution by organic solvents, 90.

F

*Fagara xanthoxyloides* gum, aldobiuronic acid from, 3166.
**Ferrocene,** derivatives of. Parts VIII—XI, 4600, 4604, 4610, 4615.
derivatives of, prep. from fulvenes, 4610.
disubstituted derivatives of, 4604.
hydroxymethyl- and hydroxyethyl-, β-glucopyranosides of, prep., 4464.
Ferrocenium thiocyanate, formation in mixed aqueous solvents, 473.
**Ferrocenes,** substituted, prep., 1827.
azo-, 4615.
tetrahydropyrido-, 4600.
**Festuclavine,** an alkaloid, isolation from *Aspergillus fumigatus* Fres., 2085.
**Fischer indole synthesis** with isopropyl methyl ketone 3-pyridylhydrazone, 584.
**Flavan derivatives.** Part IV, 499.
**Flavans,** polymerisation of. Parts IV, V, 3677, 4663.
**Flavan-3,4-diols,** 2,3-*trans*-, stereochemistry, 4663.
**Flavan-4-ols,** condensation with phenols, 3677.
**Flavone,** 7-fluoro-, and related compounds, prep., 3155.
**Flavones** and chromones. Part III, 2663.
cyano-, prep., 2663.
6-halogeno-, and related compounds, prep., 3414.
**Floridean starch,** physical properties, 1534.
**Fluorene,** compounds of, substituent effects in. Part III, 3052.
derivatives of. Part XII, 1400.
series, kinetic studies of. Part I, 2561.
2-amino-9-bromo-, hydrobromide, and related compounds, prep., 1400.
9-diazo-, acid-catalysed solvolysis of, 2561.
(+)-2-Carboxy-9-phenyl-9-phosphafluorene 9-oxide, loss of optical activity in reduction of, 2133.
Di-(9-phenyl-9-fluorenyl) peroxide, thermal decomposition, 3879.
**Fluorene,** Fluoren-10-ylacetic acid, 1,2,3,10-tetrahydro-2,8-dimethyl-3-oxo-, synthetic route to, 3958.
9-Fluorenylamine, derivatives of, prep., reactivity, and pharmacology, 1291.
**Fluorenes,** 9-chloro-9-phenyl-, hydrolysis of, 3052.
2-substituted 9-diazo-, prep., 1412.
**Fluorination** of the trioxides of chromium, molybdenum, tungsten, and uranium by selenium tetrafluoride, 3549.
**Fluorine,** organic compounds of. Parts XX—XXIII, XXV, XXVI, 3448, 3452, 3457, 3537, 4033, 4669.
Chlorine trifluoride, gaseous reaction with methane, 5449.
Diethyl fluoro-oxaloacetate, further reaction with aldehydes, 4033.
Epifluorohydrin, reactions of, 3448.
Ethyl fluoroacetate, methylene reactivity in, 3537.
Ethyl γγγ-trifluoroacetate and 5,5,5-trifluoro-4-oxopentanoic acid, cyanohydrins of, 4519.
Fluorides, complex, prep. by use of sulphur tetrafluoride as fluorinating agent, 2496.
Fluorides and oxyfluorides of molybdenum, tungsten, rhenium, and osmium, vapour pressures, 1568.
Fluorocarbon radicals, reactions. Part XVI, 3015.
Fluorocarbons, complexes with transition metals. Part I, 2738.
Halogen polyfluorides, mixtures with halogens as effective sources of the halogen monofluorides in reactions with fluoro-olefins, 3779.
Hexafluorides of heavy transition-metals, vapour pressures of, 1563.
Hexafluorocyclobutanes and pentafluorocyclobutenes, some isomeric, prep., 3198.
Keto-compounds, α-fluorinated, prep. and reactions, 3452.
Mevalonic acid, fluorine analogues, prep., 3457.
Pentafluorobenzaldehyde and related pentafluorophenyl ketones and carboxylic acids, prep., 808.
Pentafluoronitrobenzene, reaction with ammonia, 802.
Pentafluorosulphur compounds, high-resolution nuclear magnetic resonance spectra, 4736.
Perfluoroalkyl derivatives of nitrogen. Part IX, 1351.
Perfluoro-olefins, complexes with transition metals, 2738.
Perfluoro-*o*- and -*p*-xylene, prep., 1574.
Phosphonitrilic fluoride, tetrameric, crystal structure, 4777.
Polyfluoroalkylmercuric fluorides, 3825.
Polyfluoroarenes. Parts III, IV, 2204, 3719.
Polyfluoro-compounds, aromatic. Parts VII—IX, 802, 808, 1574.
Polyfluoro-compounds, heterocyclic. Part I, 1740.
Silver fluoroborate and silver hexafluorophosphate, prep., 4689.
Sodium hexafluoromolybdate(v), structure, 4253.
Sulphur chloride pentafluoride, reactions, 5554.
Sulphur chloride pentafluoride, reaction with unsaturated hydrocarbons, 2066.
reaction with fluoro-olefins, 2070.
Tetrafluorides of the sulphur sub-group, co-ordination compounds formed by, 3417.
Trifluoroacetic acid, studies of. Part XVII, 1771.
Trifluoroiodomethane, mechanism of addition to ethylene, 4973.
Trifluoromethylthiosilver, prep. and properties, 2597.
Trifluoronitrosomethane, reaction with unsymmetrical olefins, 1351.
Triphosphonitrilic 1,1-difluoride 3,3,5,5-tetrachloride, nuclear magnetic resonance spectra, 1382.
**Formals,** mixed, derived from alcohols and phenols, 2578.
**Formates,** alkyl chloro-, mechanism of hydrolysis, 3748.
**Formic acid,** thermodynamic properties, 2241.
**Friedel–Crafts** co-catalysts, relative efficiencies of halogenated acetic acids as, 1453.
reactions of camphoric anhydride in anisole and in benzene, 68.
reactions, aliphatic. Parts III, IV, 1342, 1345.
**Fries rearrangement** of half-esters from fusion of phenol and *p*-cresol with phenylsuccinic anhydride, 1083.
of *p*-tolyl acetate catalysed by zirconium tetrachloride and stannic chloride, 3842.
**D-Fructose,** di-*O*-isopropylidene-1-*O*-toluene-*p*-sulphonyl-, action of hydrazine on, 4823.

**Fulvalene**, *X*-ray determination of the crystal and molecular structure, 4936.
a hexaphenyl-, prep., 4153.
**Fulvalenes**, fulvenes, and cyclopentadienes. Parts I—III, 4153, 4158, 4162.
1,1′-dihydro-2,3,5,2′,3′,5′-hexa- and 1,1′-dihydro-2,3,4,5,2′,3′,4′,5′-octa-phenyl-, prep., 4158.
**Fulvenes**, fulvalenes, and cyclopentadienes. Parts I—III, 4153, 4158, 4162.
prep. of ferrocene derivatives from, 4610.
**Fulvic acid**, structure, 798.
prep. and reactions of degradation products, 798.
**Fungal detoxication**. Part V, 5397.
**Fungi**, chemistry of. Parts XXXVIII, XXXIX 3820, 4579.
higher, chemistry of. Part XII (Oxford school), 1532.
higher, constituents of. Parts I, II (R. L. Edwards *et al.*), 4995, 5003.
**Furan**: Dinaphtho(2′,3′-2,3)(2″,3″-4,5)furan, prep., 765.
**Furan-2,3-dicarboxylic acids**, 4,5-diaryl-, prep. from β-aroylpropionic acids, 707.
**Furfuryl alcohol**, reaction with 2,4-dinitrophenylhydrazine in methanolic hydrochloric acid, 4690.
**Furil**, conformation as solute in benzene, 4447.
**2-Furoic acid**, arylation in Meerwein's diazo-reaction, 2576.
**Fustic**, young (*Rhus cotinus*), colouring matter of the wood, 3538.

## G

**Gafrinin**, sesquiterpenoid lactone from *Geigeria africana*, isolation and structure, 2049.
**D-Galactofuranoside**, α-D-glucopyranosyl, biosynthesis, 1088.
**D-Galactose**, saccharides containing, biosynthesis by *Betacoccus arabinosaceous*, 1088.
α- and β-anomers, crystallographic examination, 3157.
amino-derivatives, prep., 2926.
di-*O*-isopropylidene-6-*O*-toluene-*p*-sulphonyl-, action of hydrazine on, 4823.
**Gallic acid**, esters and depsides of, 1836.
biosynthesis, 1854.
**Gallotannins**. Part I, introduction, 1829. Parts II—IV, 1836, 1842, 1854.
**Gamma-radiation**, effects of. Part V, 4086.
**Gedunin**, some reactions, 3705.
*Geigeria africana*, sesquiterpenoid lactone (gafrinin) from, isolation and structure, 2049.
**Geijerene**, independent confirmation of structure by physical methods, 2286.
**Geodoxin** and related compounds, oxidative coupling leading to, 2312.
**Geraniolenes**, prep., 539.
**Germanium**. Germanes, conductimetric titration with sodium in liquid ammonia, 2676.
Germanes, aryltriethyl-, cleavage by aqueous-methanolic perchloric acid, 297.
Protodetriethylgermylation, effects of strongly deactivating substituents in, 5082.
**Gibberellic acid**. Part XVIII, some rearrangements of ring A, 2498.
**Gibberellin $A_3$**, 3545.
(±)-**Gibberone**, alternative synthetic approach to, 3958.
**Glass electrode**, precise measurements of ionisation constants of benzoic, phenylacetic, and β-phenylpropionic acids, 275.
**α-1,4-Glucans**, branched, characterization of structure-type of, 1534.
**D-Glucitol** and its borate complex, partial periodate oxidation of, 1546.
**D-Glucofuranose**, 1,2-*O*-isopropylidene-, five-, six-, and seven-membered cyclic phosphates of, prep., 448.
**Glucopyranosides**, carbonium ions formed in acid-catalysed solvolysis of, structure, 3240.
**β-Glucopyranosides** of hydroxymethyl- and hydroxyethylferrocene, prep., 4464.
**β-D-Glucopyranoside**, phenyl 2-amino-2-deoxy-, and some 2-acylamino-derivatives thereof, prep., 879.
t-butyl, acid-catalysed hydrolysis of, 412.
**α-D-Glucopyranosyl D-galactofuranoside**, biosynthesis by *B. arabinosaceous*, 1088.
**α-1,4-Glucosans**. Parts XI, XII, 1183, 2681.
**Glucose**, and some of its acetyl derivatives, alkaline degradation, 531.
Guanosine diphosphate glucose, prep., 2574.
**D-Glucose**, two new cyclic phosphates of, prep., 448.
amino-derivatives, prep., 2926.
2-amino-2-deoxy-, hydrochloride of, reaction with aqueous ammonia, 2468.
4,6-*O*-benzylidene-, configuration at the benzylidene acetal carbon atom, 5005.
2-deoxy-2-sulphoamino-, and heparin and related substances, properties, 1204.
**Glucoside** (aucubin) of *Aucuba japonica*, Thunb., 5194.
**Glucosides**, aryl, variation of optical rotation with temperature, 5172.
**α-D-Glucoside**, methyl 4,6-*O*-benzylidene-3-deoxy-3-phenylazo-, prep., 4166.
**α-D-Glucosides**, substituted phenyl, acid and alkaline hydrolysis, 4291.
**Glucoxylan**, enzymic prep. of a, 3995.
**Glutamic–aspartic transaminase**, apoenzyme of, isolation from pig heart muscle, 1698.
**Glutamic acid**, reaction with nitrous acid, 3593.
steric course of lactonisation following deamination, 3278.
residues, fission of peptides containing one, 524.
**Glutamine**, reaction with nitrous acid, 3593.
steric course of lactonisation following deamination, 3278.
**Glutinane**, epoxy-, from *Rhododendron westlandii*, 551.
**Glycerol**: Bisglycerol tricarbonate, infrared spectrum, 581.
**Glycines**, *N*-aroyl-, reaction with perfluoro-carboxylic anhydrides, 1771.
**Glycogen–iodine complexes**, absorption spectra, 1183.
**Glycogens**, end-group assay by oxidation with sodium metaperiodate, 2681.
**Glycols**, polyethylene and polypropylene, of low molecular weight, dipole-moment studies, 4729.
**Glycollic acid**, tungstate and molybdate complexes with, 4732.
**Glycosides**, acid-catalysed hydrolysis of, 412.
methyl, as transfer agents in polymerisation of acrylonitrile and styrene, 3308.
**Glycosylamines**, isomeric *N*-aryl-, prep., 323.
**Graveoline** (alkaloid), prep., 4360.
**Grignard reagent** from *p*-bromodimethylaniline, prep., 465.
**Gris-2′-en-4′-ones**, 3-alkylidene-, ozonolysis products of, structure and stereochemistry, 327.
**Griseofulvin**, total synthesis, 4067.
**Guanidine**, heterocyclic derivatives of. Part II, derived products, 2098. Parts III, IV, 4332, 4672.
**Guanidines**, *N*-(thiobenzamido)-, and related compounds, prep. and cyclisation, 1617.
**Guanosine**, alkylation of, 3923.
**Guanosine diphosphate glucose**, prep., 2574.
**Guanylic acid**, alkylation of, 3923.
**Gum** exudate of *Albizzia zygia* (Macbride), structural studies, 3908.
from *Anogeissus schimperi*, constitution, 3461.
from *Fagara xanthoxyloides*, aldobiuronic acid from, 3166.
from *Virgilia oroboides*. Part II, isolation of oligosaccharides after partial hydrolysis, 4892.

## H

**Halides** of the transition elements of the first long period, physical properties, 3323.
of the transition metals, complex. Part II, 3512.
Tropylium complex halide salts of boron, aluminium, iron, titanium, and tin, 2320.
**Halogen** compounds, organic, radiation chemistry of. Part I, 4485.
substitution, aromatic, kinetics and mechanisms. Parts X, XI, 2749, 5285.
**Halogens**, mixtures with halogen polyfluorides as effective sources of the halogen monofluorides in reactions with fluoro-olefins, 3779.
Halogeno-complexes, relative stabilities. Part II, bond-strengths, 1023.
**Halogenation** of the 2-halogenobutanes, 3520.
free-radical, of t-butylbenzene, 2587.

**Hammett** reaction constant, influence of pressure on, 1093.
relation, test of: ionisation constants of some substituted anilines and phenols, 388.
σ-constants for ethyl phenylacetate and derivatives, 3247.
**Hardwoods**, extractives from. Parts XXXI, XXXII, 702, 2714.
**Heat** of autoprotolysis of sulphuric acid, 2962.
of ionization of some substituted anilines, 2572.
**Heats** of formation and bond energies. Part V, 3793.
of formation of the halides of the transition elements of the first long period, 3323.
of formation of the trimeric and tetrameric phosphonitrilic chlorides, 430.
of mixing, new calorimeter for, 3425.
of sublimation of straight-chain monocarboxylic acids, 1048.
**Hecogenin**, steroids derived from. Part II, some ring C-seco-derivatives, 3504.
**Helenin**, some reduction products of, 4721.
*Heliotropium indicum* L., major alkaloid of (indicine), 5400.
**Hemicelluloses** of roselle fibre (*Hibiscus sabdariffa*), 5262.
**Heparin**, 2-deoxy-2-sulphoamino-D-glucose, and related substances, properties, 1204.
**Heptitol**, D-*glycero*-D-*gluco*-, cyclic acetals of, structure, 3633.
**Heteroaromatic compounds**, new. Part IX, 425.
polycyclic, infrared spectra. Part II, 3983.
**Heterocyclic** analogues of conjugated cyclic hydrocarbons. Parts IV—VI, 163, 1724, 3579.
**compounds**, addition reactions of. Part VIII, 457.
of chalcone type, 2242.
polyfluoro-. Part I, 1740.
related to isatin 3-thiosemicarbazone, 243.
from urea derivatives. Part II, 5137.
**molecules**, polarographic reduction of. Part III, 5297.
**phenols**, thermochromism of, 182.
**1,12:2,3:4,5:6,7:8,9:10,11-Hexabenzocoronene**, crystal structure, 1280.
**Hex-2-enal**, an insect repellant from black cocktail ants, 488.
**Hexosides**, interaction of phenylboronic acids with, 2325.
**Hexosylamines**, *N*-aryl, paper-chromatographic investigation of transglycosylation with arylamines, 320.
**Hispidin**, prep., 5003.
a new 4-hydroxy-6-styryl-2-pyrone from *Polyporus hispidus* (Bull.) Fr., 4995.
**Histidine**, DL-α-methyl-, dihydrochloride, prep., 5037.
**Hong Kong Ericaceae**, new triterpene from, 551.
**Hopanone**, hydroxy-, final clarification of stereochemistry, 3891.
**Hormones**, steroid, compounds related to. Parts II—VII, 2532, 4531, 4535, 4547, 4560, 4573.
modified steroid. Parts XXI—XXIV, 2091, 2821, 4108, 4111.
**Hudson's lactone rule**, application to hydroxypipecolic acids: an anomaly, 4268.
**Hydantoins**, 3-alkyl-1-arylsulphonyl-, prep., 4660.
2-thio-, 3-alkyl-1-arylsulphonyl-, prep., 4660.
**Hydramine fission**, mechanism, 4576.
**Hydratropic acids** and the related 2-phenylpropanols, prep., 171.
**Hydrazine**, formation by glow-discharge electrolysis in liquid ammonia, 5177.
2,4-dinitrophenyl-, reaction with furfuryl alcohol in methanolic hydrochloric acid, 4690.
hydrate and palladium–charcoal, prep. of 1,2-dihydro-1,4-dihydroxy-2-oxoquinolines by reductive cyclisation with, 5058.
αα-Diphenyl-β-picrylhydrazyl, reactions with phenols, 2160.
Toluene-*p*-sulphonhydrazide, some unusual reactions, 4970.
**Hydrazinium(1+)** as a ligand, 4177.
**Hydrazoic acid**, direct amination of mesitylene by, in concentrated sulphuric acid, 4685.
**Hydrido-complexes** of iron(II), 5507.
of ruthenium(II) and osmium(II), 2605.
**Hydrocarbons**, reactions with hydroxyl radicals in aqueous solution, 4281.
slow oxidation in the gas phase. Part I, 4014.
**Hydrocarbons, aromatic**, action of sulphur monochloride on, 4510.
electron-transfer reactions between oxygen and, 905.
formation at high temperatures. Parts XII—XIV, 3400, 3403, 3407.
mechanism of adsorption of, by chromatographic alumina, 58.
steric effects on spectra of, 2063.
polycyclic, synthesis. Part IV, 4079.
polynitro-, complex formation in pyridine solutions of, 4886.
**arylalkyl**, homolytic substitution by thiocyanogen in, 2447.
**branched-chain**, synthesis and reactions of. Part XIV, 2587.
**conjugated cyclic**, and their heterocyclic analogues. Parts IV—VI, 163, 1724, 3579.
**polycyclic**, ozonolysis. Parts II—IV, 1232, 3858, 3864.
**polynuclear**, crystal-structure studies. Parts V, VI, 1115, 1280.
**Hydrogen bond** formation, studies in. Part X, 5434.
**bonding** of imidazole in carbon tetrachloride solution, 2165.
in aqueous solutions of maleic acid, 2790.
in solutions of 4-methyl-2,6-di-t-butylphenol, steric inhibition of, 2557.
of pyrazole, in carbon tetrachloride solution, 140.
of substituted pyrazoles in carbon tetrachloride solution. 4201.
in thiosemicarbazones and thioamides, 957.
intramolecular, in methyl 4,6-*O*-benzylidene-D-aldohexosides, 3617.
**chloride**, liquid, as an ionizing solvent. Part III, 1238.
**sulphide**, intracrystalline oxidation, 4741.
first acid dissociation constant at high pressure, 4678.
**transfer**. Part XIX, 4794.
**Hydrogenation**, catalytic, rôle of supports in. Parts I, II, 4137, 5086.
of benzene and cyclohexene over nickel in a flow system, 302.
**Hydrolysis** of acetic anhydride. Parts VI, VII, 2305, 4362.
of acid chlorides, mechanism. Part VII, 3748.
of alkyl acetates and corresponding lactones, kinetics, 47.
of esters, tracer studies in. Part IX, 943.
of phenyl and diphenylmethyl trifluoroacetate, tracer studies in, 943.
of triphenyl and trimethyl phosphates, kinetics, 2670.
acid-catalysed, of the methyl cyclohexane-mono- and -dicarboxylates and - 4-t-butylcyclohexanecarboxylates, kinetics, 2543.
acid and alkaline, of some substituted phenyl α-D-glucosides, rates, 4290.
neutral, of some allyl and benzyl halides, kinetics, 1596.
**Hydroxyl radicals**, reactions with hydrocarbons in aqueous solution, 4281.
**Hydroxylamines**, *NN*-di-(1-cyanoalkyl)-. Part I, prep., 4063.
**Hydroxylaminetrisulphonate** and hydroxylamine-*NO*-disulphonate ions, hydrolysis in perchloric acid, 3625.
**Hyoscine**, absolute configuration, 3222.
**Hyoscyamine**, absolute configuration, 3222.

I

**Imidazole**, hydrogen bonding in carbon tetrachloride solution, 2165.
some ligands containing, 4790.
Simple benzimidazoles, infrared spectra, 2343.
**Imidazoles**, purines, and pyrimidines. Parts, XV, XVI, 3254, 4845.
1-amino-, prep., 4845.
1-amino-, and derivatives. Part I, 3816.
**Imidazole-4-carboxamide**, 5-amino-2-methyl-, 1-amino-derivatives of, prep., 3816.
**Imidazoline**: 2-Oxobenzimidazoline, acyl derivatives of, 4827.
**2-Imidazolines**, 2-amino-, prep., 5120.
**Imides**: Carbodi-imides, disproportionation of, 5051.
**Indane-1,3-dione**, 2-acetyl-4,5,7-trimethoxy-, prep., 792.

XUM

**Indanone:** 2,3-Dihydro-3,3-dimethyl-1*H*-1,7-diazaindan-2-one, prep., 747.
**Indene:** 3,3′-Bi-indenyl, prep. and reactions, 1498.
**Indenes,** diaza-, and their quaternary salts. Part II, 584.
polyaza-, structure. Part VIII, 3046.
tetra-aza-, from reaction of ethyl β-ethoxy-α-ethoxycarbonylcrotonate with 3-amino-1,2,4-triazoles, 3046.
**Indeno(2′,3′:1,2)phenanthrene,** 4′-isobutyl-6′-methyl-, prep., 4320.
new prep., 3361.
**Indeno(2′,1′-2,3)thiophen,** 3′-oxo-, Schmidt reaction with: structure of the product, 1408.
**Indicine:** major alkaloid of *Heliotropium indicum* L., 5400.
**Indigo:** Iron bisindigo, a compound reported to exhibit oxygen-carrying properties, 4025.
**Indole,** 3-acetyl-, prep., 4267.
4- and 6-hydroxy-2,3-diphenyl-, 3516.
Indolylmagnesium iodides, reaction with nitroethylene, 744.
Skatole, 5-hydroxy-, prep., 746.
**Indoles.** Part V (G. F. Smith *et al.*), 940. Part VI (K. Schofield *et al.*), 5558.
3-alkyl-, dimers of, 940.
Dioxindoles prep. and conversion into *o*-aminoaryl ketones, 5558.
**Indole-4,7- and -6,7-quinone,** 2,3-diphenyl-, 3516.
**Insect repellant** from black cocktail ants, 488.
**Interaction,** molecular: molecular polarisation of amines in benzene and carbon tetrachloride, 2974.
**Intermediates,** unstable. Parts XI—XIII, 1, 7, 12.
**Iodine,** cations of, in solution, 12.
complexes of, in inert solvents. Part IX, 1200.
complexes with amylopectin and glycogen, absorption spectra, 1183.
dissolved in inert solvents, reaction with solid sodium hydroxide, 1200.
radioactive, kinetics of exchange between sodium iodide and n-butyl iodide, 226.
Iodides, Group V quaternary, iodomercurate complexes with. Part I, aqueous decompositions and absorption spectra, 3929.
Protodeiodination of *p*-iodoaniline, mechanism, 822.
Sodium iodide in acetic acid as a mild dealkylating agent, 3345.
**Ion association,** thermodynamics of. Parts VII—IX, 2215, 4367, 4458.
**Ion-exchange materials,** absorption of electrolytes by, 4784.
**Ions,** condensed, in aqueous solutions. Part II, 3211.
solvation of. Part II, 1328. Part III, $S_N2$ reactivity of some Group VI anions, pyridine, and alkyl halides in dipolar aprotic solvents, 4398.
**Ionisation constants** of benzoic, phenylacetic, and β-phenylpropionic acids at 25°, 275.
of substituted anilines and phenols: test of the Hammett relation, 388.
**Ionising radiation,** chemical action on simple aliphatic alcohols. Parts I, II, 3962, 3970.
**Ionising solvent,** liquid hydrogen chloride as. Part III, 1238.
**β-Ionone,** an oxidation product of, constitution, 308.
**Ionophoresis** of carbohydrates. Part VII, 4649.
**Ipecacuanha alkaloids.** Part VII, 3899.
indole analogues of, stereospecific prep., 3899.
**Iron,** complexes of, spectrophotometric and thermodynamic properties, 4630.
tetrahedral complexes of, prep., 3512.
cyclopentadienyl derivatives, substituted, 4619.
tropylium complex halide salts of, 2320.
Cycloheptatrieneiron carbonyl and related compounds, 594.
π-Cyclopentadienyl- and cyclopentadiene-iron carbonyl complexes, 3172.
Ferric stearate, conductance in aliphatic hydrocarbons, 466.
Iron bisindigo, a compound reported to exhibit oxygen-carrying properties, 4025.
Iron(II), hydrido-complexes of, 5507.
Iron(II), organometallic complexes of, 285.
**Isatin 3-thiosemicarbazone,** heterocyclic compounds related to, 243.
**Isatogens.** Part I, 5205.
**Isoalloxazines** related to riboflavin, prep., 476.
**Isobutane,** oxidation of, reactions during the induction period, 4014.
reaction of methoxyl radicals with, 348.
nitroso-, crystal structure of *trans*-dimer, 3686.
**Isobutyryl chloride–aluminium chloride,** interaction with decalin, 4303.
**Isoclovene,** structure: *X*-ray analysis of the hydrochloride and hydrobromide, 4382.
**Isocyanuric acid,** tris-(2-hydroxyethyl) ester, prep., 3148.
**Isodrin–aldrin series,** cyclisations and rearrangements in, 4809.
**Isodunniol,** new prep., 3548.
**Isolichenin,** structure, 623.
**Isopropenyl** and isopropylidene groups: the terpene problem, 2353.
**Isopropyl alcohol,** gaseous oxidation of. Part I, influence of temperature, pressure, and mixture composition on the formation of hydrogen peroxide and other products, 1884. Part II, influence of the surface on the formation of hydrogen peroxide and other products, 3041.
**Isopropylidene** and isopropenyl groups: the terpene problem, 2353.
**Isoquinoline,** derivatives of, reaction with acrylonitrile, 4939.
derivatives, novel prep., starting with diacylation of olefins, 3561.
**Isoquinolines,** 8-phenyl-, prep., 3882.
**Isorotenolols,** structure and stereochemistry, 2861.
**Isorotenolones,** structure and stereochemistry, 2861.
**Isoursenol,** ursane analogue of taraxerol, prep., 2638.

## K

**Kerr constant,** molar, of solutes, chloroform as solvent for determination of, 1671.
**Keto-compounds,** α-fluorinated, prep. and reactions, 3452.
**Ketones,** absorption spectra. Part VI, 1224.
reactions with lead tetra-acetate, catalysis with boron trifluoride, 4472.
reactions with oxidising agents. Part I, 4472.
ten aliphatic, as solutes in carbon tetrachloride, dipole moments, polarisations, and molar Kerr constants, 4148.
*o*-aminoaryl, conversion of dioxindoles into, 5558.
diaryl, reduction to diarylmethanes, 1405.
divinyl-, prep., 1345.
Macrocyclic bis-(1,3-diketones), prep., 5015.
**Ketoximes,** quaternary, spectroscopic studies, 2162.
**Kindler reaction,** prep. of thio-oxamides and thioamides by extensions of, 1194.
**Kinetics** of acetylation of anisole by acetic acid in presence of boron trifluoride, 1676.
of addition of trifluoroiodomethane to ethylene, 4973.
of bromination of anisoles and phenols, 63.
of bromination of ethyl malonate and methyl methanetricarboxylate, 726.
of condensation of ethyl cyanoacetate with guanidino-2*H*-pyrroles, 4332.
of detritiation of biphenyl and naphthalene, 1012.
of exchange of radioactive iodine between sodium iodide and n-butyl iodide, 226.
in studies of the fluorene series. Part I, 2561.
of hydrolysis of acetic anhydride in deuterium oxide solution, 2305.
of hydrolysis of alkyl acetates and corresponding lactones, 49.
of hydrolysis of t-butyl chloride, 1517.
of hydrolysis of hydroxylaminetrisulphonate and hydroxylamine-*NO*-disulphonate ions in perchloric acid, 3625.
of hydrolysis of triphenyl and trimethyl phosphates, 2670.
of hydrolysis of phenyl and diphenylmethyl trifluoroacetate, 943.
of acid-catalysed hydrolysis of the methyl cyclohexane mono- and -di-carboxylates and 4-t-butylcyclohexane carboxylates, 2543.
of alkaline hydrolysis and bromination of bromoform, 1413.

**Kinetics** of neutral hydrolysis of allyl and benzyl halides, 1596.
of isotopic exchange reactions between radioactive lithium chloride and benzyl and diphenylmethyl chloride, 4342.
and mechanism of substitution at the central carbon atom of tri-*p*-nitrophenylmethyl chloride in glacial and aqueous acetic acid, 5479.
and mechanisms of aromatic halogen substitution. Parts X, XI, 2749, 5285.
and mechanism of formation of a novel bicyclopentyl derivative, 1946.
and mechanism of oxidation of mandelic, DL-malic, and lactic acid by ceric sulphate, 3097.
of oxidation of benzoin with cupric citrate, 1579.
of oxidation of calcium in moist oxygen, 884.
of the reaction of alkyl and aryl compounds of the nickel group with pyridine, 2207.
of reactions of *p*-bromo-(1,2-epoxyethyl)benzene and *p*-(1,2-expoxyethyl)toluene with benzylamine, 1708.
of reaction of dichloromethylene with water and with phenoxide ions, 1663.
of reactions between ions and dipolar molecules, effect of solvent composition on. Part III, 226.
of reaction between methyl fluoride and lithium iodide in acetone solution, 1523.
of thermal decomposition of dibenzyl hyponitrite in solution, 1788.

L

**Lactic acid,** oxidation by ceric sulphate, kinetics and mechanism, 3097.
**Lactones,** enol, of β-aroyl-α-arylmethylenepropionic acids, synthesis and mechanism of isomerisation of, 1658.
**Lactone-acids,** homologous cyclic, prep., 1514.
**Lactonisation,** steric course following deamination of glutamic acid, glutamine, and γ-aminovaleric acid, 3278.
**Lanosta-5,8-dien-7-one,** 3β-acetoxy-, photoisomerisation of, 1215.
**Lanthanum dicarbide** and sesquicarbide, magnetic properties, 1775.
**Lanthionine,** polymeric polypeptides of, prep., 459.
**Lead,** dicyclopentadienyl-, 547.
mesityl and phenyl derivatives of, 4405.
tetra-acetate, reactions with ketones, catalysis by boron trifluoride, 4472.
tetra-acetate, reaction with α-pinene, 2232.
Plumbanes, aryltricyclohexyl-, cleavage by aqueous-ethanolic perchloric acid, 3715.
Plumbanes, trialkyl-. Part I, 1679.
Trimethylplumbane–borine–ammonia system, properties of, 1679.
**Lecithin,** adsorption of water vapour by, 5385.
**Leucoanthocyanidin,** new (teracacidin), from *Acacia intertexta*, 499.
**Leucoanthocyanidins** of plants. Part III, 2787.
**Leucopelargonidin** from *Eucalyptus calophylla* Kino, 2787.
**Ligands** containing imidazole, 4790.
**Ligand field** strengths of the halide, methyl, phenyl, and hydride anions, 772.
**Light absorption** of dyes, studies in. Part III, 1209.
**Lignans.** Part I, acylation in phosphoric acid as a route to intermediates, 4506.
**Limonin,** structure: *X*-ray analysis of epilimonol iodoacetate, 4183.
and related bitter principles, constitutions, 255.
**Linoleic acid,** prep., 2779, 4409, 5270.
**Linoleic acids,** substituted, prep., 3854.
**γ-Linoleic acid,** prep., 2779.
**γ-Linolenic acid,** prep., 5270.
**Liquid-phase reactions** at high pressures. Part XIII, 146.
**Liriodendritol** (an inositol ether), constitution, 4718.
**Lithium,** reaction products with mesityl oxide, 2255.
butyl-, interaction with 1,1-diphenylethylene, 4653.
n-butyl, heat of formation and bond energies, 3793.
amalgam, reactions with dihalogenonaphthalenes, 515.
iodide, reaction with methyl fluoride in acetone solution, kinetics, 1523.
**Loganin.** Part II, structural interpretation of the spectral properties, 1407.
**Lucerne** (*Medicago sativa*), pectic substances from. Part I, 4215.
**Lupane series,** dehydrogenation with mercuric acetate in. Parts I, II, 3353, 5224.
**Lupane-3β,20-diol,** prep., 2330.
**Lupeol,** and its derivatives, dehydrogenation with mercuric acetate, 5224.
and its esters, bromination, 5353.
**Lycorine,** a degradation product (1-ethyl-1,2,3,5-tetrahydro-10-methyl-7,8-methylenedioxy-5-oxobenzo[*f*]pyrrocoline) of, prep., 4350.
**Lysolecithin,** adsorption of water vapour by, 5385.
micelles, hydration, 5385.

M

**Macrocycles,** conjugated. Part XXII, 866.
*Maesopsis eminii*, constituent of (2-acetyl-1,8-dihydroxy-3-methylnaphthalene), 702.
**Magnesium:** Organomagnesium halides, unsolvated, prep., 1175.
**Magnetic perturbation** of singlet–triplet transitions. Part V, mechanism, 1987. Part VI, 2566.
**properties** of binuclear complexes, 396.
of some $d^4$ complexes, 3132; $d^3$ complexes, 3138.
(and chemical properties) of lanthanum dicarbide, 1775.
of the phosphonitrilic halides, 1376.
**susceptibility** measurements by the Gouy method, triethylenediaminenickel(II) as a calibrant for, 3147.
**Mairin,** a triterpene from *Eugenia maire* A. Cunn., 642.
identity with betulic acid, 4684.
**Malaccol,** structure and stereochemistry, 5445.
**Malachite Green,** biphenyl analogues, steric effects in, 3445.
derivatives containing substituents in the phenyl ring, electronic absorption spectra of, 1285.
derivatives containing *ortho*-substituents in the dimethylaminophenyl groups, electronic absorption spectra, 1529.
**Maleic acid,** hydrogen bonding in aqueous solutions of, 2790.
**Maleimide,** a coloured, prep. and interaction with cysteine, 2810.
**Malic acid,** tungstate and molybdate complexes with, 3691.
**DL-Malic acid,** oxidation by ceric sulphate, kinetics and mechanism, 3097.
**Malonates** of transition metals, ion association in aqueous solution, 4367.
**Malonic acid,** ethyl ester, kinetics of bromination, 726.
**Malononitrile,** condensation products with carbonyl compounds, 4705.
*Malus* species, dihydrochalcones of, 4133.
**Mandelic acid,** tungstate and molybdate complexes with, 4732.
oxidation by ceric sulphate, kinetics and mechanism, 3097.
**Mandelic acids,** use in resolution of α-hydroxyamidinium chlorides, 3181.
**Manganese:** π-Cyclohexadienylmanganese tricarbonyl and related compounds, 3807.
Manganese(II), tetrahedral complexes of, containing triphenylphosphine oxide and triphenylarsine oxide as ligands, 3735.
Manganese(II) chloride complexes. Part I, stability constants, 5148.
Nitratopentacarbonylmanganese(I), prep., 4839.
**Mannan,** from baker's yeast, 29, 3918.
**Mannich reaction** with cholesta-1,4-dien-3-one, 3059.
**α-D-Mannopyranoside,** methyl, carbonate derivatives, prep., 3178.
**D-Mannose,** carbonate derivatives, prep., 3178.
**Maytenone.** Part I, isolation and structural studies, 4420.
a degradation product of (podocarpane-6,7-diol), prep., 4430.
**Melanin,** formation from adrenochrome, 52.
**Membranes,** ion-selective, effect of pressure on transport of non-electrolytes through, 4483.
**Menschutkin reactions,** acceleration by pressure, structural effects in, 146.

XUM

**(−)-Menthyl benzoylformate** (phenylglyoxylate), reduction, 168.

**Mercury** exchange, one-alkyl, pattern of steric effects among alkyl groups and mechanisms in, 2359.
exchange reaction, one-alkyl, uncatalysed, kinetics, stereochemistry, and mechanism, 1133.
exchange reactions, one-alkyl, anion-catalysed, kinetics, stereochemistry, and mechanism, 1142.
exchange reaction, three-alkyl, kinetics, stereochemistry, and mechanism, 1121.
bis(trifluoromethylthio)-, and derived compounds, Raman spectra, 3187.
dichloro(ethylenediamine)-, infrared spectrum and structure, 477.
divinyl-, pyrolysis, 2580.
Iodomercurate complexes with Group V quaternary iodides. Part I, aqueous decompositions and absorption spectra, 3929. Part II, reactions with triphenylphosphine, 5127.
Mercuric acetate, dehydrogenation with, in the lupane series. Part I, 3353.
Mercuric fluorides, polyfluoroalkyl-, prep., 3825.

**Mesityl oxide,** reaction products with lithium, 2255.

**Mesitylene,** direct amination by hydrazoic acid in concentrated sulphuric acid, 4685.

**Mesomeric** effect, in derivatives of *NN*-dimethylaniline, steric repression of, 81.
moments of amino-, methylamino-, and dimethylamino-groups, 81.

**Mesoxalyl chloride phenylhydrazones,** cyclisation to substituted 4-hydroxycinnoline-3-carboxylic acids, 2828.

**Metal alkyl–metal halide complexes,** catalytic action of. Part I, 1733.

**Metal** chelates. Parts I, II, 869, 1257.
nitrates and nitrites, molten, surface tensions, 468.

**Metals,** cyclopentadienyl compounds with, variation of bond type in, 690.
of Group VI, cycloheptatriene complexes of, proton resonance spectra, 2037.
of Group VI, hexacarbonyls of, reactions with di- and tri-tertiary phosphines, 4980.
**alkali,** tributyl- and triphenyl-stannyl derivatives of, reactions, 618.
**transition,** heats and entropies of reaction with triethylenetetramine, 5115.
alkyls and aryls of. Part IV, 285.
complexes with a tetra-tertiary arsine, 4269.
complexes with fluorocarbons. Part I, 2738.
complex halides of. Part II, 3512.
complexes with nitric oxide. Part VI, 775.
complexes with seven-membered ring systems. Parts III, IV, 594, 2037.
ions, heats and entropies of reaction with diethylenetriamine, 2994.
oxyanions of, structure and reactivity. Part XI, 3204.
perchlorates of, infrared spectra, 3091.
heavy, vapour pressures of hexafluorides of, 1563.

**Methane,** trifluoroiodo-, mechanism of addition to ethylene, 4973.
trifluoronitroso-, reaction with some unsymmetrical olefins, 1351.
4,4′-dihydroxytriphenyl-, molecular complexes based on derivatives of, 393.
nitro-, second virial coefficients, 2247.
dinitro-, polarographic behaviour and controlled-potential electrolysis, 5325.
triphenyl-, dyes, nucleophilic replacements in, 2642.

**Methanes,** diaryl-, prep. by reduction of diaryl ketones and diarylmethanols, 1405.
di- and tri-aryl-, steric effects in. Parts III—VII, 1285, 1395, 1529, 2642, 3445.

**Methanetricarboxylic acid,** methyl ester, kinetics of bromination, 726.

**Methanol,** irradiation in the absence and in the presence of oxygen in the solid and in the liquid state, 3970.

**Methanols,** diaryl-, reduction to diarylmethanes, 1405.

**Methoxide,** ethoxide, and hydroxyl ions, comparison of the nucleophilic reactivity in dioxan, 5259.

**Methoxyl radicals,** reactions with cyclopropane and isobutane, 348.

**Methyl cation,** triphenyl-, competition for, between aniline and phenol, 575.
**chloride,** tri-*p*-nitrophenyl-, kinetics and mechanism of substitution at the central carbon atom, in glacial and aqueous acetic acid, 5479.
**fluoride,** reaction with lithium iodide in acetone solution, kinetics, 1523.
**fluoride,** reaction with lithium iodide in acetone solution, kinetics, 1523.
**group,** effect of, in aromatic detritiation, 247.
**nitrite,** pyrolysis, 3082.
**radicals,** reaction with hydrogen bromide, 3037.

**Methylamine,** *NN*-di-2-chloroethyl-, reaction with thiosulphate, 679.
thionaphthenyl-, derivatives of, prep., reactivity, and pharmacology, 1291.

**Methylation** of alkyl 3-alkyl-2,4,6-trihydroxyphenyl ketones, 1021.
of 5α-cholest-6-en-3-one, boat conformation of ring-A in steroids, 767.

**Methylene,** reaction with buta-1,3-diene, 4402.
dichloro-, reaction with water and with phenoxide ions, kinetics, 1663.

**Mevalonic acid,** fluorine analogues of, prep., 3457.

**Michler's Hydrol Blue,** α-alkyl derivatives of, electronic absorption spectra, 1395.

**Micrococcin** *P*, chemistry of. Parts V, VI, 3381, 3394.

**Mixed crystals** of ethylene dichloride and ethylene dibromide, solid transitions in, 3021.

**Molecular weight,** cryoscopic determination of, submicro-, 480.

**Molybdenum,** cyclopentadienyl derivatives, substituted, 4619.
di-π-cyclopentadienyl hydrides of, prep., 4854.
oxytetrafluoride and pentafluoride, vapour pressures, 1568.
trioxide, fluorination by selenium tetrafluoride, 3549.
Molybdate complexes with acyclic polyhydroxy-compounds, 35.
Molybdate complexes with glycollic and mandelic acid, 4732.
Molybdate complexes with tartaric, malic, and succinic acid, 3691.
Molybdenum(II) complexes containing triphenyl-phosphine oxide or -arsine oxide, 750.
Molybdenum(III) thiocyanates, complex, structure, 4590.
Molybdenum(V) chloride, reaction with aliphatic amines, 24.
Sodium hexafluoromolybdate(V), structure, 4253.

**Monascin,** structure, 4579.

**Monosaccharides** and their derivatives, sulphates of. Part II, periodate oxidation, 1692. Part III, acid hydrolysis, 2935.

**Montmorillonite,** tetramethylammonium, sorption of hydrocarbon mixtures by, 850.

**Montmorillonites,** alkylammonium, sorption of mixtures and selectivity in. Parts, I, II, 842, 850.

**Musizin** (2-acetyl-1,8-dihydroxy-3-methylnaphthalene), extraction from *Maesopsis eminii*, 702.

**Myoinositol,** cyclohexylidene derivatives of, prep., 4116.
phosphates, prep., 4122.

**N**

**Naphthalene,** detritiation, rates, 1012.
phenylation, determination of total and partial rate factors, 3112.
reaction with some aroyl peroxides, 3116.
1-1′-acetoxyvinyl-3,4-dihydro-, prep. and reactions with dienophils, 201.
2-acetyl-1,8-dihydroxy-3-methyl- (musizin), constituent of *Maesopsis eminii*, 702.
2,7-dihydroxy-, derivatives of, prep., 4258.
2-methoxy-, isobutyl and t-butyl derivatives of, 1409.

**Naphthalenes,** substituted, luminescence of, 3893.
alkyl-, heterolytic and homolytic thiocyanation of, 2436.
dihalogeno-, reactions with lithium amalgam, 515.
1,2-dihydro-, substituted, dehydrogenation by quinones, 4794.

**Naphthalenes,** ten dinitro-, quantitative study of further nitration of, 4314.
polynitro-. Part III, 4314.
**1,2-Naphthaquinones,** prep. from derivatives of 2,7-dihydroxynaphthalene, 5293.
**1,4-Naphthaquinone,** 2,3,5,7-tetrahydroxy-, prep., 1008.
**2-Naphthoic acid,** 3-nitro-, prep., 2253.
**Naphthols,** arylazo-, infrared spectra and structure, 2151.
**Naphthylamines,** *N*-acyl-nitro-, nitration of, 4859.
nitro-, and their *N*-acyl derivatives, bromination, 4866.
**1-Naphthylamines,** 4-arylazo-, dipole moments and absorption spectra, 5163.
**Neosaman,** structure, 3641.
**Nerbowdine** (buphanitine), racemisation during Oppenauer oxidations, 4038.
**Nickel** group, alkyl and aryl compounds of, kinetics of reaction with pyridine, 2207.
tritertiary arsine complexes of, 4433.
cyclopentadienyl derivatives, substituted, 4619.
Bis(triphenylphosphine)nickel dinitrosyl, prep., 2259.
Cyclopentadienylnickel–acetylene complexes, prep., 577.
**Nickel(II),** complexes with triarylphosphines, 4816.
Nickel(II), complexes with nitric oxide, prep., 775.
Nickel(II), tetrahedral complexes of, and factors determining their formation. Parts II, III, 2705, 4816.
Disalicylaldehydenickel, structure, 2594.
**Nicotine,** volatile products of pyrolysis of, 2455.
**Nicotinic acid 1-oxide,** reaction with acetic anhydride, 5216.
*Nitella translucens,* non-esterified pectic acid from, 5333.
**Nitramides** and nitramines. Part XII, 1797.
**Nitramine,** *N*-methyl-*N*-*p*-nitrophenyl-, thermal rearrangement, 2616.
**Nitramines** and nitramides. Part XII, 1797.
*ON*-dialkyl-, base catalysed decomposition, and evidence for existence of geometrical isomers, 1797.
**Nitration** of benzyl derivatives, mechanism, 2938.
of benzylic compounds by mixed acid and acetyl nitrate, *ortho* : *para* ratios in, 3888.
of biphenyl, *ortho* : *para* ratios in, 3885.
of methyl phenethyl ether, *ortho* : *para* ratio in, 3030.
further, of the ten dinitronaphthalenes, quantitative study, 4314.
**Nitriles,** reactions of. Part I, 1066.
**Nitro-group,** influence of, on side-chain reactivity. Parts I, II, 217, 221.
upon α-proton-extraction from 4-nitrobenzyl chloride, inhibition of, 221.
**Nitrogen,** carcinogenic compounds of. Part XXIX—XXXI, 384, 2258, 4836. (Part XXVIII, *J.*, 1960, 4500.)
perfluoroalkyl derivatives of. Part IX, 1351.
phosphorus compounds of. Part I, 872.
sulphur compounds with. Part II, 3625.
dioxide, liquid mixtures with nitric oxide, composition of vapour in equilibrium with, 2106.
$NMe_3$ and $ONMe_3$, anisotropies of the molecules, 2612.
Dibenzyl hyponitrite, kinetics of thermal decomposition in solution, 1788.
Dinitrogen trioxide. Part IV, 2107.
Nitrates, metal, molten, surface tension of, 468.
alkylammonium, reaction in dinitrogen tetroxide with uranium, 2987.
Nitric oxide, liquid mixtures with nitrogen dioxide, composition of vapour in equilibrium with, 2106.
transition-metal complexes with. Part VI, 775.
Nitric acid, extraction from aqueous solution by organic solvents: dimerisation of nitric acid in the organic solvent, 90.
Nitrites, alkyl, abstraction of nitric oxide from, by methyl radicals in the gas phase, 5302.
metal, molten, surface tension of, 468.
Cyclohexyl and 1-methylcyclohexyl nitrite, alicyclic alkoxyl radicals in thermal decompositions of, 2620.
Ethyl nitrite, 1-phenyl-, 1-phenylethoxyl radicals in thermal decomposition of, 4006.
Methyl nitrite, pyrolysis, 3082.
Nitrous acid, reaction with glutamine and glutamic acid, 3593.
complex formed with tributyl phosphate, 1705.
vapour, formation and thermodynamic properties, 1017.
**Nitrogen,** [$^{18}$O]Nitrous acid, deamination of cyclohexylamine by, 761.
Nitrosyl chloride, microwave spectrum, structure, and nuclear quadrupole coupling coefficients of, 1322.
Radical-ion, $NO_3^{2-}$, 7.
**Nitrosamines,** $^{14}$C-labelled dialkyl-, prep., 4226.
**Nitroso-compounds,** aromatic: molecular structure of some products from the Ehrlich–Sachs reaction, 1631.
**Non-electrolytes,** activity coefficients in aqueous solutions of sugars, 4906.
**Nucleic acids,** constituents of, infrared spectroscopic investigation, 504.
**Nucleophilic reactivity** of ethoxide, methoxide, and hydroxide ions in dioxan, a comparison, 5259.
**Nucleoside phosphites,** prep., 2316.
**Nucleotidates,** peptidyl-, prep., 2053.
**Nucleotides.** Part XLVI, 2316.

## O

**Octadec-12-enoic acid,** (±)-*cis*-9-hydroxy-, prep., 4945.
**Δ$^{1(9)}$-Octal-2-one,** tautomerism of, 4089.
**Octa-1,3,5,7-tetraene,** prep., and singlet–triplet absorption-spectrum, 2566.
**Œstra-1,3,5(10)-triene-2,3,16α,17β-tetraol,** prep., 4769.
**Œstra-1,3,5(10)-trien-17-one,** 2,3-dihydroxy-, prep., 4769.
**Œstrogens,** 2-hydroxy-. Part II, 4769.
**Olefins,** reaction with acylium perchlorates, 3573.
complexes with rhodium, observations on, 1418.
compounds with diboron tetrachloride. Part III, 356.
conformationally fixed. Part III, 1650.
cyclic, diacylation of, and novel prep. of isoquinoline derivatives, 3561.
fluoro-, reaction with sulphur chloride pentafluoride, 2070.
perfluoro-, transition/metal complexes with, 2738.
pyrylium salts obtained by diacylation of. Parts II—IV, 3553, 3561, 3564.
and sulphides, co-oxidation of, 5339.
***cis*-Olefinic acids,** pure, attempts to prepare, 351.
**Olefinic, additions,** with asymmetric reactants. Part VI, 670.
**Oleic esters,** rôle of peroxides in autoxidation of, 4324.
**Optical rotatory dispersion.** Part II, 545.
**Optical studies** of 2,2′-di-t-butylbiphenylcarboxylic acids and of 2′-t-butylbiphenyl-2-carboxylic acid, 611.
**3*d*-Orbitals,** role in π-bonds between (*a*) silicon, phosphorus, sulphur, or chlorine and (*b*) oxygen or nitrogen, 5486.
**Organic reactions** in aqueous solution at room temperature. Part II, 5211.
**Organometallic compounds,** reactions with dithizone, 1470.
of Group II. Part III, 1175.
**Osage orange,** triterpene constituents of the fruits of. Part II, 2330.
**Osmium** pentafluoride, vapour pressure, 1568.
Osmium(II), complexes of tertiary phosphines with, prep., 896.
Osmium(II), hydrido-complexes, prep., 2605.
**Osotriazoles** from carbohydrates, scope and mechanism of formation. Parts V, VI, 2957, 3146.
chloro- and iodo-phenyl-, prep., 2957.
**Oxalates** of transition metals, ion association in, 2215.
**Oxalic acid,** oxidation with quinquevalent vanadium, 4757.
**Oxaloacetic acid.** Part I, nature in the solid state and in neutral aqueous solution, 5043.
**Oxamides,** infrared spectra, 1919.
thio-, infrared spectra, 1919.
thio-, prep. by extensions of the Kindler reaction, 1194.
**1,3-Oxazines,** derivatives of, infrared spectra and structure, 489.
**Oxazoles,** 4-substituted, reactions of, 405.
**Oxazolidine-2,5-diones,** 3-substituted, polymerization of, 2057.
**2-Oxazolines,** 2-amino-, prep., 5120.
**Oxidation–reduction potentials** of copper complexes, 2007.
**Oxidations,** competitive. Parts II, III, 782, 4285.
at low temperatures induced by light, competitive, 4285.
of organic compounds by cupric salts. Part II, 1579.
of organic compounds with quinquevalent vanadium Parts VII, VIII, 630, 4757.

**N-Oxides and related compounds.** Part XVIII, 43.
**Oxyanions** of transition metals, structure and reactivity. Part XI, 3204.
**Oxygen,** organic compounds of, thermodynamic properties. Parts II, III, 2236, 2241
**Ozonolysis** of polycyclic hydrocarbons. Parts II—IV, 1232, 3858, 3864.

P

**Palladium,** tritertiary arsine complexes of, 4433.
catalysts, activation effects of various oxide carriers on, 4137.
difluoride and complex fluorides of palladium, prep. in selenium tetrafluoride, 3728.
Palladium(II), complexes with nitric oxide, prep., 775.
Palladous [$^{36}$Cl]chloride, decomposition of, 639.
**Pectic acid** from lucerne (*Medicago sativa*), 4215.
non-esterified, from *Nitella translucens*, 5333.
**substances** from lucerne (*Medicago sativa*). Part I, 4215.
**Pentanoic acid,** 5,5,5-trifluoro-4-oxo-, cyanohydrins of, 4519.
(±)-**Pent-3-en-2-ol,** 4-phenyl-, dissymmetric hydrogenation of, 670.
D-**Pentoses,** 2-acetamido-2-deoxy-, epimerization, 1577.
**Pentyl.** See t-pentyl.
**Peptides** containing one glutamic acid residue, fission of, 524.
and proteins, degradative studies. Part VI, 3161.
**Peptide links,** specific chemical fission of. Part III, 524.
**Peptidyl-nucleotidates,** prep., 2053.
**Periodate oxidation.** Part VI, 2525.
**Peroxides,** rôle in the autoxidation of elaidic acid and oleic esters, 4324.
of elements other than carbon. Part VII, 341.
organic. Parts V, VI (J. I. G. Cadogan *et al.*), 3879, 5236. Part X (A. G. Davies *et al.*), 4390.
*p*-nitrophenyldiphenylmethyl, decomposition, 5236.
**Pharmacodynamic compounds.** Part II, 633.
**Phenanthrene,** kinetics and mechanism of chlorination in acetic acid, 5285.
free-radical phenylation of, 73.
Indeno(2′,3′:1,2)phenanthrene, new prep., 3361.
Indeno(2′,3′:1,2)phenanthrene, 4′-isobutyl-6′-methyl-, prep., 4230.
**Phenanthrenes,** 1,2,3,4-tetrahydro-9,10-diaza-, attempted prep. from cyclohexane-1,2-dione monophenylhydrazones, 4256.
**Phenanthridine,** 10-methyl-, prep., 2249.
αω-Di(phenanthridin-6-yl)alkanes, prep., 3664.
*N*-Methylbenzophenanthridones, independent prep. and formation by internuclear cyclisation, 3873.
**Phenanthridines,** cyclisation of biphenyl derivatives to, 3771.
**Pheniramine,** resolution of, 2228.
**Phenol,** competition with aniline for triphenylmethyl cation, 575.
vibrational assignment and calculated thermodynamic properties, 2236.
4-amino-2-methoxy-, ethers of, prep., 1863.
4-methyl-2,6-di-t-butyl-, steric inhibition of hydrogen-bonding in solutions of, 2557.
4-nitro-2,6-di-t-butyl-, prep. and thermal decomposition, 953.
2,4-dinitro-, equilibria with mono-, di-, and tri-n-butylamine in aprotic solvents, 417.
**Phenols,** biosynthesis of. Part III, 2312.
bromination of, kinetics, 63.
*o*-amino-, stability constants of metal complexes of, 2244.
heterocyclic, thermochromism of, 182.
new, prep., 2773.
substituted, ionisation constants of, 388.
*ortho*-substituted, association with ethers, 4762.
**Phenolic radicals,** oxidative pairing of. Parts I, II, 4067, 4075.
**Phenoxide ions,** reaction of dichloromethylene with, kinetics, 1663.
**Phenyl peroxide,** di-*p*-(2-amino-2-carboxyethyl)-, prep. from tyrosine and probable natural occurrence in proteins, 3193.
**Phenylation** of naphthalene, determination of total and partial rate factors, 3112.
of nitrobenzene, relative rate of, redetermination, 565.
free-radical, of phenanthrene, 73.
*p*-methyl-, of nitrobenzene and chlorobenzene, 3108.
**Phospholipids.** Part VII, 3774.
**Phosphorus,** analogues of aminodiarylboranes, prep., 1000.
heterocyclic compounds of, synthesis and stereochemistry. Part II, 2133.
nitrogen compounds of. Part I, 872.
organic acids of, anhydrides. Part II, 4904.
organic compounds of. Parts I—III (Z. Pelchowicz *et al.*), 238, 241, 4348.
organic compounds of, reactivity. Parts IV—X (J. I. G. Cadogan *et al.*), 3067, 3071, 3076, 3079, 5524, 5532, 5542.
esters, reaction with carbonyl chloride, 3067.
$PCl_3$ and $OPCl_3$, anisotropies of the molecules, 2612.
pentachloride, interaction with tertiary amines, 1730.
pentoxide–calcium oxide system, high-temperature studies of, 4442.
phosphoric anhydride, tri- and tetra-alkyl esters, prep., 4904.
Bis(triphenylphosphine)nickel dinitrosyl, prep., 2259.
Boranes, phosphino-aryl-, 5053.
Borines, dialkylphosphino-, trimeric, and some *B*-halogenated derivatives, prep. and infrared spectra, 1822.
Calcium hydrogen phosphate precipitated from solutions of calcium nitrate and phosphoric acid, stability, 4914.
Cobalt(III) ammine phosphates, phase-diagram studies of, 86.
Cyclotetraphosphonitrile, octamethyl-, crystal structure, 5471.
Cyclotriphosphazatriene, alkylamino- and dialkylamino-derivatives of, prep., 872.
Ethyl ethylphosphonothiolate, concerted action of fluoride and silver ions on, in aqueous solution, 4624.
Hypophosphate, prep. and determination, 1079.
Hypophosphate, dithionate, and related ions, vibrational spectra and structures, 1552.
Inositide, a monophospho-, structure, 3774.
Orthophosphoric acid, and water, rates of oxygen exchange between, 1636.
9-Phosphafluorene 9-oxide, (+)-2-carboxy-9-phenyl-, loss of optical activity in reduction of, 2133.
**Phosphates,** reactions with *O*-benzenesulphonyl-lactims, 1641.
cyclic, prep. from cyclic phosphites, 710.
cyclic, of D-glucose, prep., 448.
cyclic, of 1,2-*O*-isopropylidene-D-glucofuranose, five-, six-, and seven-membered, 448.
organic, reactions of. Parts IV, V, 1636, 2670.
trialkyl, interaction with boron trichloride, 4095.
trialkyl, reaction with sodium *NN*-diethyldithiocarbamate, 3164.
trialkyl, interaction with silicon chlorides, 4680.
trialkyl, reaction with thiourea, 442.
tri-n-alkyl, radiolysis of, 4098.
triphenyl and trimethyl, hydrolysis, 2670.
Dibutyl phosphate–potassium perrhenate–aqueous nitric acid system, heterogeneous equilibria in, 5046.
Guanosine diphosphate glucose, prep., 2574.
Tributyl phosphate–nitrous acid complex, 1705.
Tributyl phosphate–potassium perrhenate–aqueous nitric acid system, heterogeneous equilibrium in, 1921.
**Phosphine,** conductimetric titration with sodium in liquid ammonia, 2676.
dibutylphenyl- and butyldiphenyl-, tetrahedral nickel(II) complexes with, 2705.
triphenyl-, adducts with dimethyl acetylenedicarboxylate, 2126.
*o*-Phenylenebis(diethylphosphine), reaction with metals, 5504.
**Phosphines,** 1-hydroxyalkyl-, rearrangement to alkylphosphine oxides, 2813.
tertiary, complexes with ruthenium(II) and osmium(II), 896.
di- and tri-tertiary, reactions with the hexacarbonyls of metals of Group VI, 4980.
triaryl-, complexes with nickel(II), 4816.

**Phosphorus: Phosphines,** Diphosphine dioxides. Part II, 2423.
Diphosphine dioxides with mono-, di-, and tri-methylene bridges, prep., 2423.
**Phosphine oxide** complexes. Parts IV, V, 2298, 3735.
triphenyl-, as ligand in tetrahedral complexes of manganese(II), 3735.
triphenyl-, molybdenum(II) complexes containing, 750.
**Phosphine oxides,** complexes with copper(II), prep., 2298.
alkyl-, rearrangement of 1-hydroxyalkylphosphines to, 2813.
Phosphinimine, *N*-methyltrichloro-, dimer, prep., 1825.
**Phosphites,** ammonium alkyl hydrogen, prep., 5050.
cyclic, oxidation to cyclic phosphates, 710.
dialkyl, reactions of alkali derivatives of, 4348.
dialkyl, reaction with sodium *NN*-diethyldithiocarbamate, 3164.
dialkyl, reaction with thiourea, 442.
organic, reactions with chloramine-T, 3079.
trialkyl, reaction with trichloromethyl radicals, 3071.
triaryl, conductance of solutions in, 311.
Nucleoside phosphites, prep., 2316.
Phosphobetaines, prep. and properties, 1266.
containing a basic group, use in Wittig reaction, 2130.
phosphonates, methyl-, and methylphosphonothionates, dialkyl, reaction with inorganic acid chlorides, 238.
Phosphonic dichloride, triphenylmethyl-, structure, 3542.
**Phosphonitrilic** chlorides, trimeric and tetrameric, heats of formation of, 430.
derivatives. Parts IV—VII, IX, 430, 1768, 1825, 4777, 5471. (Part VIII, *J.*, 1962, 635.)
fluoride, tetrameric, crystal structure, 4777.
halides, delocalization and magnetic properties, 1376.
Triphosphonitrilic fluoride chlorides, prep., 1768.
Triphosphonitrilic 1,1-difluoride 3,3,5,5-tetrachloride, nuclear magnetic resonance spectra, 1382.
**Phosphonium** halides, alkyltriphenyl-, reduction with lithium aluminium hydride, 4263.
salts containing a basic group, use in Wittig reactions, 2130.
salts, arsino-, prep., 3208.
Phosphor- and phosphon-amidates, *N*-chloro-, prep., 3076.
Phosphoramidic acids, *N*-acyl-, hydrolysis of. Part IV, *N*-benzenesulphonylphosphoramidic acid, 3158.
**Phosphoric acid,** effect of pressure on first acid dissociation constant of, 1765.
acid esters of, reaction with acetimidates, 1805.
alkyl esters, solvent-extraction of beryllium from aqueous solutions of mineral acids by, 174.
Phosphoric acid–chromium(III) system, phase diagram at 70° and ion-exchange studies in, 291.
Phosphorothioites, dialkyl, and their reaction with chloral, 241.
Phosphorothiolates, reaction with alkyl iodides, 5542.
Triethyl phosphorothiolate and related compounds, reactions with chloramine-T, 5524.
Phosphorothionates, reaction with alkyl iodides, 5532.
Phosphoryl chloride–boron trichloride complex, structure, 4255.
Propionic esters, β-(diarylphosphino)-, abnormal hydrolysis. Part I, 5454.
Pyrophosphate ion, $P^1P^1$-diethyl, existence of, 4321.
Silver hexafluorophosphate, prep., 4689.
Sugars, phosphorylated. Part III, 448.
**Phosphorylation.** Parts XXII, XXIII, 715, 722.
oxidative, experiments on, 1808.
**Photochemical transformations.** Part XI, 3313.
**Photochromism** in some spiropyrans. Part III, 156.
**Phototransformation** in spiropyrans, extent of, 156.
**Phthalimides,** thio-, prep., 5055.
**Phthalocyanines,** absorption spectra of, 866.
**Phthalocyanine complex,** micromethod for determination of valency of a metal in, 869.
**Phthalocyanine–chromium complexes** and perpendicular conjugation, 1257.
**Physical properties** and chemical constitution. Part XXXII, 570.
**3-Picoline 1-oxide,** reaction with acetic anhydride, 5216.
**Picolinic acid,** silicon esters of, co-ordination in, 3897.
**Picrates,** metho-, double, of certain heterocyclic tertiary amines, prep., 3845.
**Picrolichenic acid,** prep., 4075.
**Picrotoxin** and tutin. Parts XI, XII, 3000, 3006.
**Pimaric acid,** sandaraco- and crypto-, constitution, 752.
**Pinacol** and its monomethyl ether, kinetic resemblance between oxidations of α-hydroxy-acids and, 630.
**Pinacols,** mixed, prep. by cathodic reduction. Part II, 2081.
symmetrical, prep. by cathodic reduction, 757.
**α-Pinene,** reaction with lead tetra-acetate, 2232.
**Pipecolic acid,** 4-hydroxy-, from *Acacia* species, and its stereoisomers, 189.
**Pipecolic acids,** hydroxy-, application of Hudson's lactone rule to: an anomaly, 4268.
**Piperidine–pyrrolidine series,** rearrangements in, 633.
**Plant growth-regulating compounds,** relationship of structure to activity in. Part I, 2335.
**Platinum** catalysts, effects of various oxide supports on the activity of, 5086.
tritertiary arsine complexes of, 4433.
"Cyclopropane platinous chloride," structure, 738.
Ethylene-platinous chloride pyridine *N*-oxide, 2254.
$PtCl_4^{2-}$–$I^-$ and $PtBr_6^{2-}$–$I^-$ replacement reactions, 2981.
Platinum(II), complexes with acetylenes. Part I, alkynes, 827.
Platinum(II), complexes with nitric oxide, prep., 775.
Platinum(II), five-co-ordinate complexes of, prep., 3699.
Platinum(II), thiocyanato-bridged complexes of, 1416.
**Plutonium** trifluoride and tetrafluoride, solubility in nitric acid mixtures, 2464.
tetrafluoride, vapour pressure, 2031.
Plutonium(IV) oxalate, solubility in nitric acid mixtures, 2464.
**Podocarpane,** 7,8-dimethoxy-, prep., 4425.
**Podocarpane-6,7-diol,** prep., 4430.
8-isopropyl-(6-hydroxytotarol), prep., 4425.
**Polar effects,** transmission through aromatic systems. Parts I, II, 2221, 2938. Part III, Hammett σ-constants, 3247.
**Polarisability,** molecular, 1671, 2356, 2612, 4140, 4144, 4148, 4447.
**Polarization,** dielectric, of some imperfect polar gases, 5511.
molecular, of amines in benzene and carbon tetrachloride, 2974.
bonding, molecular complexes exhibiting. Part III, 494.
**Polarographic** behaviour of 2-methyl-1,2-di-3′-pyridylpropan-1-one, 1420.
behaviour and controlled-potential electrolysis of 1,1-dinitroethane and dinitromethane, 5325.
reduction of carbohydrates, 3487.
reduction of some heterocyclic molecules. Part III, 5297.
**Polyacetylenes** in *Polyporus anthracophilus*, 1654.
biosynthesis. Parts III, IV, 1654, 3544.
rate of synthesis by Basidiomycete B.841, 3544.
**Polyanion equilibria** in aqueous solution. Part I, 5317.
**Polyazaindenes,** structure. Part VIII, 3046.
**Polycyclic systems.** Parts IX, X, 3361, 4230.
**Polyelectrolytes,** influence of counter-ion fixation on molecular weight and shape of, 3974.
**Polyhydroxy-compounds,** acyclic, complexes with molybdate, 35.
**Polymer,** deeply coloured, electrically conducting, mechanism of formation, 1964.
**Polymers,** deeply coloured, electrically conducting, prep. and properties, 1953.
and monomers containing Sn–O–As(v), prep., 445.
**Polymerisation** of epoxides. Part III, 4298.
**Polynuclear compounds.** Part I, 396.
**Polypeptides.** Parts VI, VII, 1749, 1752.
polymeric, of lanthionine, prep., 459.
**Polyporic acid series** (potential anti-tumour agents), prep., 936.
*Polyporus anthracophilus*, polyacetylenes and triterpenes in, 1654.
*Polyporus hispidus* (Bull.) Fr., a new 4-hydroxy-6-styryl-2-pyrone (hispidin) from, 4995.
**Polysaccharides** of baker's yeast. Parts IV, V, 29, 3918.
from the green seaweeds of *Caulerpa* spp. Part III, 3010.
of the Characeae. Parts I, IV, 2914, 5333.
sulphated, estimation of relative amounts of isomeric sulphate esters in, 5168.

**Poly-*p*-xylylene** and related polymers, prep., 1604.
**Porphins,** tetraza-, absorption spectra of, and formation of pyridine salts from, 866.
*Porphyra umbilicalis*, a red alga, carbohydrates from, 1590.
**Porphyrins,** proton magnetic resonance spectra. Part I, 3468.
effect of β-substitution on the proton chemical shifts of, 3468.
formation by cyclisation of bilenes, 2418.
**Porter–Silber reaction,** 2027.
**Potassium** hydrogen di-*p*-nitrobenzoate, crystal structure, 1151.
**Prednisolone,** 9α-fluoro-16β-methyl- prep., 4560.
**Pregna-5,9(11),16-trien-20-one,** 3β-hydroxy-, prep. from botogenin, 1859.
**Pregn-4-ene-3,20-dione,** 16α,17α-isopropylidenedioxy-6α-methyl-, prep., 4111.
**5α-Pregn-9-ene-3,20-dione,** 21-acetoxy-17-hydroxy-16β-methyl-, partial synthesis, 4547.
**Prodine,** alpha- and beta-, action of thionyl chloride on alcohols derived from, 5057.
**Progesterone,** 6α,16α-dimethyl- and 17α-acetoxy-6α-methyl-16-methylene-, prep., 2821.
**Propane,** 2,2-dinitro-, reduction processes, studied by controlled-potential electrolysis, 4773.
**Propanols,** 2-phenyl-, related to the hydratropic acids, prep., 171.
**Propan-2-ol,** 1-chloro-3-fluoro-, reactions of, 3448.
**Propan-1-one,** 2-methyl-1,2-di-3′-pyridyl-, polarographic behaviour, 1420.
**Propiolic acid,** methyl ester, reaction with pyridine, 3497.
2-methoxy-4- and -5-methylphenyl-, prep. and reactions, 2528.
**Propiolic acids,** phenyl-. Part VII, 2528.
**Propionic acid,** β-(diarylphosphino)-, esters, abnormal hydrolysis. Part I, 5454.
β-(2,5-dimethylbenzoyl)-α- and -β-phenyl-, conversion into polynuclear compounds, 2701.
β-(8-oxo-2-tetralyl)-, attempt to cyclise, 2520.
β-phenyl-, ionisation constant at 25°, 275.
**Propionic acids,** β-aroyl-. Parts XVIII—XX, 707, 1083, 2701.
β-aroyl-, conversion into 4,5-diarylfuran-2,3-dicarboxylic acid, 707.
β-aroyl-α-arylmethylene-. Part II, prep. and mechanism of isomerisation of their enol lactones, 1658.
**Propionyl chloride,** interaction with decalin and aluminium chloride, 4306.
**Propylene oxide,** polymerization by sodium alkoxides, 4298.
**Protactinium-**(IV) and -(V), absorption spectra in certain solutions, 3804.
**Proteins** and peptides, degradative studies. Part VI, 3161.
probable natural occurrence of di-*p*-(2-amino-2-carboxyethyl)phenyl peroxide, 3193.
study of *N*-terminal residues in, 3254.
**Pteridine,** derivatives of. Part VIII, 476.
studies. Parts XIII—XV, 127, 4413, 5131.
2-amino-4-hydroxy-, and related compounds, methylation, 4413.
2-hydroxy-, reduction, 5131.
**Pteridines,** 6-hydroxy-, addition to, 127.
**Purines,** pyrimidines, and imidazoles. Parts XV, XVI, 3254, 4845.
8-substituted, prep., 4468.
9-amino-, prep. from 1-aminoimidazoles, 4845.
chloro- and others, prep. by a novel cyclisation of 4,5-diaminopyrimidines, 5048.
9-dimethylamino-, prep., 3818.
**Pyran,** tetrahydro-2-hydroxymethyl-, silyl ethers of, 5256.
**Pyrans,** spiro-, photochromism in. Part III, 156.
**Pyranoquinolines.** Part II, 2796.
**Pyrazine:** Pyrido(2′,3′-2,3)pyrazines, 5,6-dipyridyl-, prep., 2258.
**Pyrazole,** hydrogen bonding of, in carbon tetrachloride solution, 140.
3-methyl-1,5-diphenyl-, monosulphonation products, 3851.
**Pyrazoles,** substituted, hydrogen bonding in carbon tetrachloride solution, 4201.
aryl-, sulphonation of. Part I, 3851.
**Pyrazoles,** bromo-1-phenyl-, orientation of, 2769.
4-formyl-1-phenyl-, prep. and reactions, 2733.
**Pyrazolo[3,4-*d*]pyrimidines,** 1- and 2-β-D-ribofuranosyl-, prep., 2589.
**Pyridine,** reaction with methyl propiolate, 3497.
4-amino-, influence of steric factors on properties of derivatives of, 3939.
pentafluoro-, prep., 1740.
2-, 3-, and 4-methanesulphonamido-, basicities and spectra, 378.
2,3-dimethyl- and 2,4,6-trimethyl-, isolation from coal tar by a new method, 5556.
Ethyl 2- and 4-pyridylacetate, condensation with aromatic compounds, 5074.
Ethylene-platinous chloride pyridine *N*-oxide, 2254.
Isopropyl methyl ketone 3-pyridylhydrazone, cyclisation of, 584.
2,2′-Pyridil dioxime and 2,2′-bipyridyls, quaternary derivatives of, 759.
**Pyridines,** potentially tautomeric. Part III, 378.
substituted, electric dipole moments of, 4522.
4-substituted, proton nuclear magnetic resonance spectra of, 43.
**Pyridine-1-oxide,** free-radical substitution of, 18.
**Pyridine 1-oxides,** proton nuclear magnetic resonance spectra of, 43.
substituted, electric dipole moments of, 4522.
**Pyridones,** prep. from pyrones, 4490.
**2-Pyridones,** and related systems, estimation of aromatic character by nuclear magnetic resonance spectroscopy, 859.
1-hydroxy- and 1-amino-, prep. from pyrones, 4490.
**Pyrido(2′,3′-2,3)pyrazines,** 5,6-dipyridyl-, prep., 2258.
**Pyridoxal,** non-enzymic reaction with alanine, 4235.
phosphate, formation of a thiazolidine derivative in aqueous solution with L-cysteine, 4051.
**Pyridoxamine,** non-enzymic reaction with pyruvic acid, 4235.
**Pyrimidine** reactions. Part III, 1298.
4-amino-6-hydroxy-, and related compounds, methylation product of, 1298.
4,5-diamino-2-hydroxy-, simple route to, 760.
**Pyrimidines,** purines, and imidazoles. Parts XV, XVI, 3254, 4845.
Pyrazolo[3,4-*d*]pyrimidines, 1- and 2-β-D-ribofuranosyl-, prep., 2589.
**Pyrolysis,** studies in. Part XVI, 1782.
of n-butane, rôle of surfaces in, 4128.
**Pyrone series.** Part IV, 4490.
**2-Pyrone,** a new 4-hydroxy-6-styryl- (hispidin), from *Polyporus hispidus* (Bull.) Fr., 4995.
**2-Pyrones,** 5-aryloxy-, prep., 4490.
4,5,6-triphenyl-, prep., 4490.
**Pyrrocoline:** 1-Ethyl-1,2,3,5-tetrahydro-10-methyl-7,8-methylenedioxy-5-oxobenzo[*f*]pyrrocoline, prep., 4350.
**2*H*-Pyrroles,** guanidino-, prep., 4672.
guanidino-, condensation with ethyl cyanoacetate, stoicheiometry and kinetics, 4332.
**Pyrrole-1-carboxylate,** methyl, reaction with dimethyl acetylenedicarboxylate, 457.
**Pyrrolidine–piperidine series,** rearrangements in, 633.
**Pyrylium salts** and related compounds. Part I, 3573.
reaction with alkali cyanides, 3566.
formed in diacetylation of 2-methylbut-2-ene, 3553.
obtained by diacylation of olefins. Parts II—IV, 3553, 3561, 3564.

## Q

*op′*-**Quaterphenyl,** prep., 748.
**Quebracho tannin extract,** occurrence of 2-benzyl-2-hydroxycoumaran-3-ones in, 3234.
**Queen substance** (*trans*-9-oxodec-2-enoic acid), prep., 3813.
**Quinaldine,** reaction with sulphuric acid, 1098.
**Quinapyramine** (Antrycide), bisquaternary salts related to, 5275.
**Quinazoline,** cation, hydrated, structure, 5267.
cations of, 2689.
1,4- and 3,4-dihydro-, prep., 2697.

**Quinazolines.** Parts I—III, 2689, 2697, 5267.
**Quinazolinium salts,** amidinophenyldiazoamino-, prep., 4041.
**Quinic acid,** 3-*O*-*p*-coumaroyl-, prep., 5153.
**α-Quinindones,** 2,3-dihydro-, prep., 4295.
**Quinol,** hydroxy-, derivatives of. Parts II, III, 792, 798.
phosphates, phosphorylation accompanying oxidation of, 715.
monophosphates, prep. from vitamin $K_1$, ubiquinone, and other quinones, 1808.
**Quinoline series.** Part II, 1098.
3-acetyl-4-hydroxy-, derivatives of, prep. of pyranoquinolines from, 2796.
8-hydroxy-, complexes with dibutyl- and diphenyl-tin radicals, 756.
ethiodide, polarographic reduction, 5297.
Quinapyramine (Antrycide), replacement of the quinoline nucleus by other heterocycles, 5275.
**Quinolines,** 1,2-dihydro-1,4-dihydroxy-2-oxo-, prep. by reductive cyclisation with hydrazine hydrate and palladium–charcoal, 5058.
6-methoxy-8-(ω-piperazin-1′-ylalkylamino)-, prep., 2404.
1*H*-Cyclopenta[*c*]quinolines, 2,3,4,5-tetrahydro-4-oxo-, prep., 4295.
Pyranoquinolines. Part II, 2796.
**Quinolinium salts,** amidinophenyldiazoamino-, prep., 4041.
**Quinolizines:** 3-Alkyl-1,3,4,6,7,11b-hexahydro-9,10-dimethoxy-2*H*-benzo[*a*]quinolizines, 2-ketones and 2-alcohols derived from, new prep., 4711.
**Quinones,** naturally occurring. Parts IV, V, 485, 1008.
dehydrogenation of substituted 1,2-dihydronaphthalenes by, 4794.
**1,2-Quinones,** prep. from derivatives of 2,7-dihydroxynaphthalene, 5293.
**Quinoxalines** and related compounds. Part V, 1246.
1,2-dihydro-2-oxo-, experiments with, 1246.
2,3-dipyridyl-, prep., 2258.
**Quinoxaline-2,3-diones,** infrared spectra, 3983.

## R

**Radiation,** ionizing, chemical action on simple aliphatic alcohols. Parts I, II, 3962, 3970.
**γ-Radiation,** see Gamma-radiation.
**Radiation chemistry** of azide solutions. Parts I, II, 1479, 1487.
of carbohydrates. Parts VII, VIII, 3756, 3763.
**Radical-ions,** $SO_2^-$ and $NO_2^{2-}$, 7.
**Radicals,** alkoxy. Part I, 1788.
**Reactivity,** aromatic. Parts XII—XXI, 297, 247, 542, 1012, 2388, 3715, 4921, 4927, 5077, 5082.
**Rearrangements,** molecular. Part VI, 2616.
**Redox-transfer,** chlorine activation by. Part I, 2261.
**Refraction,** double, electric, of solutions containing optically active solutes, 2356.
**Reimer–Tiemann reaction,** "abnormal", applications of, 2251.
**Reserpic acid,** methyl ester, suppression of 1,3-diaxial interaction in, during alkaline hydrolysis, 4252.
**Resolution** of α-hydroxy-amidinium chlorides by the use of mandelic acids, 3181.
**L-Rhamnose,** 2,5-di-*O*-methyl-, prep., ionophoresis, and conversion into 6-deoxy-2,5-di-*O*-methyl-L-altrose, 4649.
**Rhenium,** septivalent, solvent extraction of. Parts I—III, 1921, 1926, 5046.
oxyfluorides and pentafluoride, vapour pressures, 1568.
System, aqueous nitric acid–potassium perrhenate–dibutyl phosphate, heterogeneous equilibria in, 5046.
System, aqueous nitric acid–potassium perrhenate–tributyl phosphate, heterogeneous equilibria in, 1921.
System, aqueous nitric acid–potassium perrhenate–"tri-iso-octylamine", heterogeneous equilibria in, 1926.
**Rhodanines,** 3-substituted, and their thiazine analogues, prep., 3733.
**Rhodium,** complexes with olefins, observations on, 1418.
*Rhododendron westlandii*, an epoxyglutinane from, 551.
*Rhus cotinus* wood (young fustic), colouring matter of, 3538.
**D-Ribitol,** 4-*O*-(β-D-glucopyranosyl)-, a degradation product of the ribitol teichoic acid from walls of *Bacillus subtilis*, prep., 2180.
**Riboflavin,** new prep., 476.
**1- and 2-β-D-Ribofuranosylpyrazolo[3,4-*d*]pyrimidines,** prep., 2589.
**D-Ribose,** 2-acetamido-2-deoxy-, prep. from derivatives of 3-acetamido-3-deoxy-D-altrose, 1463.
**Ring systems,** fused seven-membered, structural and conformational aspects in, 1429.
**Roselle fibre** (*Hibiscus sabdariffa*), hemicelluloses of, 5262.
**Rotenoids,** B/C-ring system, 2876.
relative stereochemistry, 1448.
Sumatrol and malaccol, structure and stereochemistry, 5445.
**Rotenolols,** structure and stereochemistry, 2861.
**Rotenolones,** structure and stereochemistry, 2861.
**Rotenone,** absolute configuration, 2843.
**Rubidium hydrogen di-*o*-nitrobenzoate,** crystal structure, 1151.
**Rubropunctatin,** further evidence for structure, 3820.
**Rutaceae** of Hong Kong, examination of. Part VII, the essential oils, 3551. Part VIII, 4360.
**Ruthenium,** alkyl, aryl, and hydrido-complexes of, ultraviolet spectra to determine ligand field strengths of some anions, 772.
nitrosyl-, complexes of, deformation frequencies of OH groups in, 4444.
Ruthenates and perruthenates, spectra, 5039.
Ruthenium red, cation, 2000.
Ruthenium(II), hydrido-complexes, prep., 2605.
Ruthenium(II), complexes of tertiary phosphines with, prep., 896.

## S

**Salicylaldehyde:** Disalicylaldehydenickel, structure, 2594.
**Salicylaldehydes,** substituted, infrared spectra, 3372.
**Salicylic acids** and their esters, substituted, infrared spectra, 661.
**Salts,** acid, of some monobasic acids, crystal structures. Parts V, VI, 1151, 1164.
**Sandaracopimaric acid,** constitution, 752.
**Sapogenins,** steroidal. Part XL, 1859.
12-oxo-, reaction with selenium dioxide, 1859.
**Sarcosine,** *N*-phenylthiocarbamoyl-, derivatives of, cyclisation and degradation, 3161.
**s-Butyl chloride,** pyrolysis of, and direction of eliminations from s-butyl compounds, 2756.
**Schistosomiasis,** chemotherapy of. Part IV, 1863.
**Schmidt reaction** with 3′-oxoindeno(2′,1′-2,3)thiophen: structure of the product, 1408.
**Scymnol,** anhydro-, and scymnol sulphate, 2817.
**β-Sedoheptitol** (D-*glycero*-D-*gluco*heptitol), cyclic acetals of, structure, 3633.
**Selenium** tetrafluoride, fluorination of the trioxides of chromium, molybdenum, tungsten, and uranium by, 3549.
tetrafluoride, prep. of palladium difluoride and complex fluorides of palladium in, 3728.
oxychloride, interaction with the trichlorides of boron and aluminium, 3165.
Diselenocarbamic acids, *NN*-dialkyl-, derivatives of, prep., 2922.
**Semicarbazides and thiosemicarbazides,** 4-substituted 1-amidino-, prep. and cyclisation, 5137.
**Semicarbazones,** thio-, hydrogen bonding in, 957.
**Semiquinones,** polycyclic, and their derivatives, electron-spin resonance spectra and odd-electron distribution, 4273.
**Serine,** enzymic resolution of, 763.
**Shellolic acid,** confirmation of structure, 5251.
**Side-chain reactivity,** influence of nitro-group upon. Parts I, II, 217, 221.
**Silicon** chlorides, interaction with trialkyl phosphates, 4680.
esters of picolinic acid, co-ordination in, 3897.
halides, reactions with sulphoxides, 3224.
tetranitrate, 1:2 addition compound with pyridine, and related compounds, 4249.
Disilthiane, hexamethyl-, reactions with alcohols, thiols, acids, and amines, 4933.
Disilylcyanamide, prep. and properties, 4879.
Silane, ethylthiotrimethyl-, reactions with alcohols, thiols, acids, and amines, 4933.

XUM

**Silicon** Silicates, hydrothermal chemistry. Parts IX, X, 971, 983.
Silicates, nitrogenous alumino-, hydrothermal chemistry, 971.
Silyl ethers of tetrahydro-2-hydroxymethylpyran, 5256.
System $CaO$–$Al_2O_3$–$SiO_2$–$H_2O$, hydrothermal study, 983.
Trialkylsilyloxides and silanols, infrared spectra, 2601.
Trimethylsilyl derivatives of diphenyl ether, diphenyl sulphide, furan, thiophen, benzothiophen, dibenzofuran, dibenzothiophen, and 9-ethylcarbazole, acid cleavage, 4921.
**Silver** complexes of some *NN*-substituted 2-hydroxyethylamines, stability constants, 3169.
fluoroborate, prep., 4689.
trifluoromethylthio-, prep. and properties, 2597.
hexafluorophosphate, prep., 4689.
**Skatole**, 5-hydroxy-, prep., 746.
**Sodium azide**, action of *X*-rays (200 kv) on deærated aqueous solutions of, 1479; in the presence of different organic solutes, 1487.
**borohydride**, reduction of 1,2- and 1,3-diketones, 910.
**hydrogen diacetate**, crystal structure, 1164.
*Solanum*, some species of, constituents, and a reassessment of solasodamine and solauricine, 4645.
alkaloids. Part XV, 4645.
**Solasodamine**, constitution, 4645.
**Solauricine**, constitution, 4645.
**Solids**, active, production by thermal decomposition. Part XIII, 1252.
**Solubilities** in liquid hydrogen chloride of derivatives of Groups IV, V, and VI, 1238.
**Solvation of ions**. Part II, 1328.
**Solvent-extraction** of beryllium from aqueous solutions of mineral acids, by alkyl esters of phosphoric acid, 174.
of nitric acid from aqueous solution, 90.
of septivalent rhenium. Parts I—III, 1921, 1926, 5046.
**Solvolysis** of γ-phenyltetronic acid enol esters, mechanism. Parts I, II, 5421, 5430.
$S_Ni$, in 50% aqueous acetone, activation parameters for, 2045.
**D-Sorbitol**, aqueous solutions in oxygen, action of γ-radiation on, 3756.
deærated solutions of, action of γ-radiation on, 3763.
**Soret effect**, optical studies of. Part I, modified optical beam-displacement method and its application to aqueous silver nitrate, 3432.
**Sorption** of mixtures, and selectivity in alkylammonium montmorillonites. Parts I, II, 842, 850.
**Spectra**: aromatic hydrocarbons, steric effects on, 2063.
inorganic complexes in non-aqueous solvents. Part I, 5105.
**absorption**: biliverdin, 2264.
copper and iron complexes, 4630.
dithizones, mono- and di-*p*-bromo-substituted, and their metal complexes, 2118.
dyes in solution and adsorbed in solid films, 1209.
glycogen– and amylopectin–iodine complexes, 1183.
ketones. Part VI, 1224.
tetrazaporphins and phthalocyanines, 866.
Singlet–triplet transitions, magnetic perturbation of. Parts V, VI, 1987, 2566.
**charge-transfer**, intramolecular, and intensified $n \longrightarrow \pi^*$ transitions, in benzo-homologues of bicyclo[2,2,2]octenone, 1224.
**electronic absorption**: Malachite Green derivatives containing substituents in the phenyl ring, 1285.
Malachite Green derivatives containing *ortho*-substituents in the dimethylaminophenyl groups, 1529.
Michler's Hydrol Blue, α-alkyl derivatives of, 1395.
**electron-spin resonance**: ·$CH(CO_2H)$·$CH_2$·$CO_2H$ in γ-irradiated DL-aspartic acid hydrochloride, 4264.
aryl carboxylic acids and their esters, 106.
polycyclic semiquinones and their derivatives, 4273.
**infrared**: aliphatic nitro-alcohols. Part I, 1370.
quaternary aldoximes and ketoximes, 2162.
arylazonaphthols, 2151.
benzamide, $^{18}O$-labelled, 1688.
*N*-methylbenzamide, normal and $^{18}O$-labelled, 2666.
*NN*-dimethylbenzamide, normal and $^{18}O$-labelled, 3063.
**Spectra, infrared**: simple benzimidazoles, 2343.
$^{18}O$-labelled benzoic acid, benzoyl chloride, and methyl benzoate, 2382.
borazoles and boroxoles, 1931.
dichloro(ethylenediamine)-zinc, -cadmium, and -mercury, 477.
cobalt(III) ethylenediamine complexes. Part II, 471.
cycloheptatrieneiron carbonyl and related compounds, 594.
dicyclopentadienyl-tin and -lead, 547.
hemialdal esters, 2525.
a bisglycerol tricarbonate, 581.
polycyclic heteroaromatic compounds. Part II, 3983.
some metal alkoxides, trialkylsilyloxides, and related silanols, 2601.
metal carbonyls and their derivatives, solvent shifts in, 2582.
chelate metal–ethylenediamine, complexes, 1112.
nitrosylruthenium complexes, deformation frequencies of OH groups in, 4444.
nucleic acid constituents, 504.
diolefincobalt carbonyl complexes, 602.
oxamides and thio-oxamides, 1919.
1,3-oxazine derivatives, 489.
alkyl-substituted phenols (OH stretching frequencies), 4762.
trimeric dialkylphosphinoborines and *B*-halogenated derivatives, 1822.
pyridine 1-oxides, 18.
quinoxaline-2,3-diones, 3983.
salicylaldehydes (substituted), 3372.
substituted salicylic acids and their esters, 661.
sulphonamidopyridines, 378.
thiazoles, 3381.
compounds containing the thiocyanate group, 471.
thiosemicarbazones and thioamides, 957.
some transition-metal perchlorates, 3091.
**luminescence**, some substituted naphthalenes, 3893.
**microwave**, of nitrosyl chloride, nuclear quadrupole coupling coefficients from, 1322.
**nuclear magnetic resonance**: studies in. Part IV, 1625.
study of aromaticity. Part I, 859.
configuration at the benzylidene acetal carbon atoms in 4,6-*O*-benzylidene-D-glucose and 1,3-*O*-benzylidene-L-arabinitol, 5005.
bisbenzylisoquinoline and aporphine alkaloids, structural correlations in, 1896.
cycloheptatrieneiron carbonyl and related compounds, 594.
the di-π-cyclopentadienyl hydrides of tantalum, molybdenum, and tungsten, 4854.
*cis*-1,2-difluoroethylene, 743.
4-substituted pyridines and pyridine 1-oxides, 43.
2-pyridones and related systems, 859.
triphosphonitrilic 1,1-difluoride 3,3,5,5-tetrachloride, 1382.
high-resolution, of pentafluorosulphur compounds, 4736.
**proton resonance**, of cycloheptatriene complexes of Group VI metals, 2037.
**proton magnetic resonance**: structure determination of bicyclopentyl derivatives from cyclopentadiene, 1939.
porphyrins. Part I, 3468.
**Raman**, of bis(trifluoromethylthio)mercury and derived compounds, 3187.
**ultraviolet**: quaternary aldoximes and ketoximes, 2162.
bromobenzo[*c*]cinnolines, 5029.
benzo-homologues of bicyclo[2,2,2]octenone, 1224.
4-arylazo-1-naphthylamines, 5163.
chromate ions (monosubstituted), 3204.
polycyclic cinnolines and their *N*-oxides, 1363.
absorption of isolated double bonds, 2075.
polymerizing systems (of styrene), 734.
protactinium-(IV) and -(V) in certain solutions, 3804.
sulphonamidopyridines, 378.
alkyl, aryl, and hydrido-complexes of ruthenium, 772.
silicon esters of picolinic acid, 3897.
**vibrational**, of dithionate, hypophosphate, and related ions, 1552.
**visible**, of dimethinecyanine salts, 163.

**Spectroscopy,** nuclear quadrupole resonance, chemical applications of. Part IV, transmission of the electronic effect of various substituents by a phosphorus atom, 2459.
**Spinels,** effect of defect structure on rate of formation of, 2745.
**Spinochromes E and N** (quinones), prep., 1008.
**Spirans.** Part III, 327.
**Spiropentane** (spirobicyclopropane), thermal isomerization, 5550.
**Spiropyrans,** photochromism in. Part III, 156.
**25D-Spirostan-6α-ol,** 3α,5-cyclo-6β-methyl-, 1821.
**25D-Spirostan-6β-ol,** 3α,5-cyclo-6α-methyl-, prep., 1821.
**Stability constants** of metal complexes of *o*-aminophenols, 2244.
of manganese(II) chloride complexes, 5148.
**Starches,** physicochemical studies on. Part XXIII, 1534.
**Starch-type polysaccharide** from *Nitella translucens*, 2914.
**Stearic acid,** ferric and cupric salts, conductance of, in aliphatic hydrocarbons, 466.
**Stereochemical structure,** studies in. Part XIV, 3181.
**Stereochemistry,** aspects of. Parts VI—IX (A. B. Foster *et al.*), 2338, 3633, 5005, 5011. Part XVIII (H. B. Henbest *et al.*), 4478.
of molecules containing the C=C=N group. Part III, 2801.
**Steroid** hormones, compounds related to. Parts II—VII, 2532, 4531, 4535, 4547, 4560, 4573.
hormones, modified. Parts XXI—XXIV, 2091, 2821, 4108, 4111.
3-ketones, pentacyclic structures from derivatives of, 4108.
sapogenins. Part XL, 1859.
**Steroids.** Part CLXIX, 4057.
examples of boat conformation of ring-A: methylation of 5α-cholest-6-en-3-one, 767.
and Walden inversion. Parts XLVII—XLIX, 1583, 3261, 3271.
of unnatural configuration. Part VI, 4676.
derived from hecogenin. Part II, some ring C-seco-derivatives, 3504.
4-substituted, by rearrangement and reduction of cholestenone enol acetate, 2478.
Aza-. Part II, 3641.
3-monohydroxy- and 3,17-dihydroxy-, and derivatives, optical rotatory dispersion, 5415.
4,4-dimethyl-, 3-epimeric toluene-*p*-sulphonates, prep., 3261.
Porter–Silber reaction, nature of, 2027.
**$\Delta^{1,4}$-Steroids,** 3,11-diketones, dienone–phenol rearrangement of, 4535.
3-oxo-, phenolic ethers from dienone–phenol rearrangement of, 4531.
**$\Delta^{8(11)}$-Steroids,** prep. from 11β-trifluoroacetates, 4573.
**$\Delta^{1}$-5α-Steroids,** 2-bromo-3-oxo-, action of hydrogen bromide on, 2532.
**Stilbenes,** α-alkyl-β-ethynyl-, prep. of acetylenic alcohols from, 1311.
α-alkyl-β-ethynyl-4,4′-dihydroxy-, prep., 2291.
*cis*- and *trans*-3,3′,4,4′-tetramethoxy-, prep., 2592.
**Stilbœstrol,** acetylenic compounds related to. Parts III, IV, 1311, 2291.
**Streptomycin,** tautomeric forms of, 1337.
**Styrene,** cationic polymerization of. Parts I—III, 729, 734, 737.
polymerization of, by aluminium chloride, cocatalytic action of water in, 737.
methyl glycosides as transfer agents in polymerisation of, 3308.
α-methyl-, prep. of 2-phenylbutadiene from, 370.
poly-(*m*-amino-), and the copolymer with styrene, 3708.
Poly-(*m*-styrenediazonium chloride) and related diazonium chlorides, kinetics of decomposition of, 3708.
**Submicro-methods** for organic analysis. Part XIII, 480.
**Substituents** in an aromatic nucleus, cumulative effect on reactions of the side chain, 4744.
**Substitution,** aromatic, *ortho* : *para*-ratio in. Parts I—V, 3030, 3604, 3610, 3885, 3888.
aromatic halogen, kinetics and mechanisms. Parts X, XI, 2749, 5285.
**Substitution,** aromatic homolytic. Parts XXI—XXVI, 554, 562, 565, 3108, 3112, 3116.
electrophilic, at a saturated carbon atom, mechanism. Parts III—VI, 1121, 1133, 1142, 2359.
free-radical, in aliphatic compounds. Part III, 3520.
free-radical, of pyridine 1-oxide, 18.
nucleophilic, at a saturated carbon atom, dipolar aprotic solvents as media for, 1328.
nucleophilic, concomitant first- and second-order, 4342.
patterns of monosubstituted benzene derivatives, 3153.
**Succinates** of transition metals, ion association in, 4458.
**Succinic acid,** tungstate and molybdate complexes with, 3691.
**Succinimide,** *N*-bromo-, action on 1,2,3,4-tetraphenylcyclobutane, 479.
**Sucrose,** carbonic esters of. Parts I—III, 5359, 5365, 5370.
**Sucroses,** *O*-alkyloxycarbonyl-, prep., 5359.
polymerisation, 5365.
**(Sucrose carbonates),** poly-, direct prep. from sucrose, 5370.
**Sugar** alcohols, prep. of αω-di-*O*-methanesulphonyl derivatives, 3656.
series, mechanisms of reactions in. Parts III, IV, 412, 3240.
**Sugars,** characterisation as *p*-*p*′-nitrophenylazobenzoyl derivatives, 5544.
aqueous solutions, activity coefficients of non-electrolytes in, 4906.
amino-, and related compounds. Part VIII, 1204.
phosphorylated. Part III, 448.
**Sulphones,** *o*-alkyldiphenyl, action of aluminium chloride on, 4514.
**Sulphonhydrazides,** rearrangement of, 1743.
**Sulphoxides,** reactions with some Group III and IV halides, 3224.
**Sulphur,** nitrogen compounds with. Part II, 3625.
chloride pentafluoride, reactions, 5554.
reaction with unsaturated hydrocarbons, 2066.
reaction with fluoro-olefins, 2070.
monochloride, action on aromatic hydrocarbons, 4510.
tetrafluoride as fluorinating agent for prep. of complex fluorides, 2496.
trioxide, condensed phases of. Part I, vapour pressure and viscosity of the liquid phase at low temperatures, 2348.
α-(Benzoylmethylthio)acetic acids, structural factors leading to either carbanion–sulphenium fission or benzoyl elimination by action of alkalis, 2393.
Diethylsulphonyl-(2-*O*-methyl-α-D-arabopyranosyl)methane, prep. and behaviour with base, 5561.
Dithionate, hypophosphate, and related ions, vibrational spectra and structures, 1552.
Hydrogen sulphide, intracrystalline oxidation, 4741.
Hydrogen sulphide, first acid dissociation constant at high pressure, 4678.
*p*-Nitrophenylmethylthio-acids, structural factors leading to either carbanion–sulphenium fission or α-proton extraction in, 2397.
4-Nitrophenylthio-derivatives of acetic, propionic, and related acids, mechanism of base-catalysed elimination from, 223.
Pentafluorosulphur compounds, high-resolution nuclear magnetic resonance spectra, 4736.
Radical-ion, $SO_3^-$, 7.
Sulphides formed from *o*-nitrobenzenesulpheny chloride and ketones, prep. and oxidation of, 367.
Sulphides (thioethers), carbon–sulphur fission in. Parts V—VII, 2393, 2397, 2402.
Sulphides (thioethers), carbanion–sulpheniun fission in, kinetics and mechanism, 2402.
Sulphides, organic, oxidation. Part X, 5339.
Sulphides and olefins, co-oxidation of, 5339.
Sulphuric acid, heat of autoprotolysis, 2962.
"Sulphurous" acid, effect of pressure on first acid dissociation constants of, 1765.
Tetramethylethylene sulphate, prep., 2257.
Thiocyanate group, compounds containing, infrared spectra, 471.
Thiocyanato-bridged complexes of platinum(II), 1416.
Thiosulphate, reaction with *N*-methyldi-(2-chloroethyl)-amine, 679.
Thiolsulphates, phenacyl, condensation with diazonium salts, 4266.

**Sulphur**, Trisulphides, new prep., 4850.
**Sulphur sub-group**, co-ordination compounds formed by tetrafluorides of, 3417.
**Sumatrol**, structure and stereochemistry, 5445.
**Supinine**, alkaloid from seeds of *Trichodesma zeylanicum*, R. Br., 484.
**Surface tension** of molten metal nitrates and nitrites, 468.
**Sydnones**, chemical and physical properties, 3303.

T

**Tannase**, fractionation of, 1829.
**Tannic acid**, a probable component of (trigallic acid), 3231.
**Tannin**, Quebracho, occurrence of 2-benzyl-2-hydroxycoumaran-3-ones in, 3234.
**Tannins**, Chinese, Turkish, Sumach, and Tara, constitution, 1842.
of tara, *Caesalpinia spinosa* (Mol.) Kuntze, 3786.
gallo-. Parts I—IV, 1829, 1836, 1842, 1854.
introduction, 1829.
**Tanshinones**. Part I, prep. of an isomer of tanshinone-I, 5090.
**Tantalum**, di-$\pi$-cyclopentadienyl hydrides of, prep., 4854.
**Tara**, tannins of, 3786.
**Taraxerol**, ursane analogue of (isoursenol), prep., 2638.
**Tartaric acid**, tungstate and molybdate complexes with, 3691.
(−)-di-*O*-*p*-toluoyl-, characterisation of amines by, 4675.
**Tautomerism** in the solid state. Parts I, II, 182, 1191.
**Tazettine**, stereochemistry of the hemiketal moiety of, 2485.
treatment with acetic anhydride and sulphuric acid, structure of products, 1055.
**t-Butyl chloride**, hydrolysis of, kinetics, 1517.
**group**, effect of, in aromatic detritiation, 247.
**peroxide**, thermal and photochemical decomposition in anisole, 5239.
*N*-**t-butylamine**, *N*-methyl-, improved prep., 4226.
**Teichoic acid** from the walls of *Bacillus subtilis*, prep. of 4-*O*-(β-D-glucopyranosyl)-D-ribitol a degradation product of, 2180.
**Teracacidin**, new leucoanthocyanidin from *Acacia intertexta*, 499.
**Terpene problem**: isopropenyl and isopropylidene groups, 2353.
**Terpenes**, studies in synthesis of. Parts VI, VII, 3251, 4211.
*p*-**Terphenyl**, isomer ratios for the mononitration in acetic acid and acetic anhydride, 5156.
*p*-**Terphenyls**, new di- and tri-nitro-, prep., 1069.
**Testosterone**, 16α-methyl- and 16β-methyl-, prep., 4057.
**Tetrabenzo-[2,2]-paracyclophane**, 3741.
**Tetralone**: β-(8-Oxo-2-tetralyl)propionic acid and γ-(8-oxo-2-tetralyl)butyric acid, attempted cyclisation, 2520.
**Tetronic acid**, γ-phenyl-, enol esters, mechanism of solvolysis. Parts I, II, 5421, 5430.
γ-phenyl-, enol acetate, methanolysis of, 5430.
γ-phenyl-, enol benzoate, conductimetric study of methanolysis of, 5421.
**Thallium**: Thallous–thallic reaction, evidence for a single-stage two-electron exchange, 5549.
**Thenylamine**, derivatives of, prep., reactivity, and pharmacology, 1291.
**Thermochemical studies**. Parts IV, VI, 2994, 5115.
**Thermochemistry** of organoboron compounds. Part VI, 2472.
**Thermochromism** of heterocyclic phenols, 182.
**Thermodynamic** properties of organic oxygen compounds. Parts II, III, 2236, 2241.
treatment of electrolyte absorption by an ion-exchange resin, 4784.
**Thermodynamics** of ion association. Part VII—IX, 2215, 4367, 4458.
**Thiadiazoles**. Part XI, 1617.
**Thiamine chloride hydrochloride**, 6-methyl-, prep., 2595.
**Thiazine** analogues of 3-substituted rhodanines, prep., 3733.
**Thiazole**: Benzothiazole, nitration, quantitative study, 2825.
**Thiazoles**, infrared spectra, 3381.
**Thiazole-4-carboxylic acid**, 2-(1-amino-2-methylpropyl)-, racemisation and related studies, 3394.
**Thiazolidine** derivative, formation in aqueous solution from pyridoxal phosphate and L-cysteine, 4051.
**Thiazoline**: 3-Methylbenzothiazoline-2-thione, crystal and molecular structure, 4379.
**Thioamides**, prep. by extensions of the Kindler reaction, 1194.
hydrogen bonding in, 957.
**Thiocyanogen**, thiocyanates, and isothiocyanates. Part I, 2447.
chloride. Parts IV, V, 2428, 2436.
chloride, reaction with aromatic hydrocarbons; heterolytic and homolytic substitution in benzene homologues, 2428.
**Thioethers**, kinetics and mechanism of carbanion–sulphenium fission in, 2402.
carbon–sulphur fission in. Parts IV—VII, 223, 2393, 2397, 2402.
**2-Thiohydantoins**, 3-alkyl-1-arylsulphonyl-, prep., 4660.
**Thiols** from reduction of 2-bromo-1,1-di-*p*-alkoxyphenylethylenes by thiophenols, addition to 1,1-di-*p*-alkoxyphenylethylenes, 2684.
**Thio-oxamides**, infrared spectra, 1919.
prep. by extensions of the Kindler reaction, 1194.
**Thiophen** compounds, physical properties and chemical constitution, 570.
oxide, tetrahydro-, complexes with metals, 2078.
Indeno(2′,1′-2,3)thiophen, 3′-oxo-, Schmidt reaction with: structure of the product, 1408.
So called "2-triacetylthiophen" (a boron compound), prep., 746.
**Thiophens** related to vitamin A, prep., 650.
**Thiophenol**, *p*-(*NN*-di-2-chloroethyl- and *p*-(*NN*-di-2-bromoethyl-amino)-, derivatives of, prep., 2375.
**Thiophthalimides**, prep., 5055.
**2-Thiopyrones**, prep. from pyrones, 4490.
**Thiosemicarbazones**, hydrogen bonding in, 957.
**Thiosuccinimides**, prep., 5547.
**Thiourea**, reaction with dialkyl phosphites and trialkyl phosphates, 442.
*S*-(2-hydroxyethyl)-, derivatives of, 5191.
**Thioxanthones**, some chemotherapeutic, physicochemical properties, 5381.
**Thiyl radicals**. Part I, 1304.
L-**Threitol**, reaction with acetone, 5095.
di-*O*-benzylidene-, structure, 5011.
*Thujopsis dolabrata*, constituents of leaves of, 4247.
D-**Thyronine**, 3,5-dichloro-, prep.: an unexpected Walden inversion, 2651.
**Thyronines**, prep. from iodonium salts and derivatives of 3,5-disubstituted tyrosines, 2645.
**Thyroxine** and related compounds, prep. Parts XV—XVII, 2645, 2651, 2890.
**Timbers**, West African. Part IV, 3705.
**Tin**, tropylium complex halide salts of, 2320.
halides, reactions with sulphoxides, 3224.
Dibutyl- and diphenyl-tin radicals, 8-hydroxyquinoline complexes of, prep., 756.
Dicyclopentadienyltin, infrared spectrum and structure, 547.
Organotin cations occurrence of, 2585.
Sn–O–As(v) linkages, preparation of monomers and polymers containing, 445.
Stannane, kinetics of decomposition on a tin surface, 2569.
Stannanes, aryltricyclohexyl- and aryltrimethyl-, rates of cleavage by aqueous-ethanolic perchloric acid, 542.
Stannic chloride, comparison of aliphatic and aromatic carboxylic acids as Friedel–Crafts co-catalysts for, 3822.
Stannous chloride dihydrate, crystal structure, 3954.
Tetrachloro-1,4-bistriethylstannyloxybenzene, crystal and molecular structure, 5027.
Tin(II), chelates formed with certain amino-polycarboxylic acids, 2554.
Tin(II) nitrate, basic, prep., 1996.
Tin(II) oxide, red, prep., 839.
Tin(II) oxide [tin(II) hydroxide], hydrous, prep., 835.
Tributyl- and triphenyl-stannyl derivatives of alkali metals, reactions of, 618.

**Titanium,** n-tetra-alkoxy- and n-alkoxy-chloro-derivatives, association of, 2947.
cyclopentadienyl derivatives, substituted, 4619.
tropylium complex halide salts of, 2320.
Hexahalogenotitanates, ammonolysis of, 95.
Titania, ion-free hydrous, calcination of, 1252.
**Titration,** spectrophotometric, of the bile pigments, 2276.
**Toluene,** [o- and $p$-$^3H_1$]-, relative reactivities in detritiation, 4927.
$p$-(1,2-epoxyethyl)-, kinetics of reaction with benzylamine, 1708.
2,3,4,5,6-pentafluoro-, and related compounds, prep., 3719.
**Toluene-$p$-sulphonhydrazide,** some unusual reactions, 4970.
**$p$-Tolyl acetate,** Fries rearrangement catalysed by zirconium tetrachloride and stannic chloride, 3842.
**Totarol,** 6-hydroxy-(8-isopropylpodocarpane-6,7-diol), prep., 4425.
3-Oxototaryl methyl ether, prep., 3319.
**t-Pentyl alcohol,** decomposition in gas phase, catalysed by hydrogen chloride, 1392.
**Transaminase,** glutamic–aspartic, apoenzyme of, isolation from pig heart muscle, 1698.
**Transamination.** Parts I, II, 1698, 4235.
**Transglycosylation** of $N$-arylhexosylamines and arylamines, paper-chromatographic investigation of, 320.
**Transitions,** singlet–triplet, magnetic perturbation of. Part V, mechanism, 1987. Part VI, 2566.
**Triazines:** Benzo-1,2,3-triazines, substituted, reactions of, 4930.
**Triazole carboxylic acids,** apparent dissociation constant of, 3146.
**1,2,4-Triazoles.** Part II, 518.
3-alkyl-5-aryl-, prep., 518.
3-amino-, preparation of tetra-azaindenes from, 3046.
*Trichodesma zeylanicum*, R.Br., seeds of, alkaloid (supinine) from, 484.
**Trigallic acid,** probable component of tannic acid, 3231.
**1,3,5-Trioxan,** pyrolysis, 1403.
**Triterpene,** new, from Hong Kong Ericaceae, 551.
constituents of the fruits of the osage orange (*Maclura pomifera*). Part II, 2330.
**Triterpenes** and related compounds. Parts XXXVIII—XLI, 646, 2725, 3891, 5353.
in *Polyporus anthracophilus*, 1654.
**Triterpenoids.** Part XXV (D. H. R. Barton *et al.*), 255. Part LVIII (F. S. Spring *et al.*), 2638.
pentacyclic, with diene unsaturation in ring c, photochemistry, 3313.
**Trögers base** as a solute in benzene, dipole moment, molar Kerr constant, and space formula of, 4144.
**Tropane alkaloids,** stereochemistry. Parts XIII, XIV, 3219, 3222.
**(−)-Tropic acid,** absolute configuration, 3222.
**Tropylium** complex halide salts of boron, aluminium, iron, titanium, and tin, 2320.
isocyanate (*alias*), [actually *NN'*-di(cyclohepta-2,4,6-trienyl)urea], prep., 482.
**Tropylium–** and cycloheptatriene–metal complexes. Parts I—III, 3475, 3479, 3484.
**Trypanocides,** new, search for. Part VI, 4041.
**Tryptamine,** 5-hydroxy-, prep., 2919.
**Tryptamines,** 5-fluoro-, $N$-alkylated, prep., 5418.
**Tumour inhibitors** from plant sources. Part I, 2599.
**Tungsten,** di-$\pi$-cyclopentadienyl hydrides of, prep., 4854.
oxytetrafluoride, vapour pressure, 1568.
trioxide, fluorination by selenium tetrafluoride, 3549.
$(PW_{12}O_{40})^{3-}$ and related ions, structure, 3796.
Tungstate complexes with glycollic and mandelic acid, 4732.
Tungstate complexes with tartaric, malic, and succinic acid, 3691.
Tungstate solutions, acidified, quantitative analysis of, 5317.
**Tutin,** structure, 3006.
**Tutin and picrotoxin.** Parts XI, XII, 3000, 3006.
**Tyrosine,** prep. of di-$p$-(2-amino-2-carboxyethyl)phenyl peroxide from, 3193.
**Tyrosines,** 3,5-disubstituted, prep. of thyronines from, 2645.

U

**Ubiquinone,** prep. of quinol monophosphate from, 1808.
**Uracils,** acetyl-, prep. from amines and amino-acids, 3254.
**Uranium,** reaction with solutions of alkylammonium nitrates in dinitrogen tetroxide, 2987.
and uranium compounds, reactions with nitrosyl chloride, and with liquid nitrosyl chloride–dinitrogen tetroxide mixtures, 2490.
trioxide, fluorination by selenium tetrafluoride, 3549.
Alkylammonium uranyl nitrates, 2987.
Bis(dibenzoylmethanato)uranyl complex, heats of solvation of, 4250.
Uranium(IV) nitrates, 4060.
Uranyl, co-ordinative power of. Part IV, 4250.
Uranyl sulphate, adsorption from 20% methanol by an anion-exchange resin, 1819.
**Urea,** derivatives of, heterocyclic compounds from. Part II, 5137.
*NN'*-di(cyclohepta-2,4,6-trienyl)-, *alias* tropylium isocyanate, prep., 482.
**Uric acid riboside** (ribosyluric acid). Part I, isolation and reinvestigation of structure, 963.
**Uridine-5′ phosphate,** L-arginyl-L-alanyl-L-arginyl-L-alanyl, prep., 2053.
**Uronic acid materials,** studies on. Part IV, 5230.
**Uronic acids,** aqueous decarboxylation and decarboxylation of pectic materials during extraction, 5230.
**Ursane analogue** (isoursenol) of taraxerol, prep., 2638.

V

**Valeric acid,** $\gamma$-amino-, steric course of lactonisation following deamination, 3278.
**Valeroidine,** absolute configuration and simplified prep., 3219.
**Vanadium,** quinquevalent, oxidation of organic compounds with. Parts VII, VIII, 630, 4757.
quinquevalent, compounds with orthophosphate, 3211.
**Veratraldehyde,** some experiments based on, 3151.
**Verdinoid pigment,** prototropy of bilirubin to, 2268.
**(±)-Vernolic acid,** prep., 5270.
**Vinyl:** Divinylmercury, pyrolysis, 2580.
**Vinylideneamine,** $N$-ethyl-2,2′-dimethylsulphonyl-, crystal and molecular structure, 2801.
*Virgilia oroboides* gum. Part II, isolation of oligosaccharides after partial hydrolysis, 4892.
**Virial coefficients,** second, of nitromethane, 2247.
**Vitamin A,** prep. of thiophens related to, 650.
**Vitamin $K_1$,** prep. of quinol monophosphate from, 1808.
*Vitex agnus castus* seeds, constituents of. Part I, 2523.

W

**Walden inversion** and steroids. Parts XLVII—XLIX, 1583, 3261, 3271.
**Washburn numbers** in the methanol–water–hydrochloric acid system at 25°, 5308.
**West African timbers.** Part IV, 3705.

X

**Xanthate,** sodium ethyl, reactions with ethanol and with water, 117.
**Xanthohumol** (a chalcone), structure, 1021.
**Xylans,** degradation by alkali, 3667.
**Xylene,** perfluoro-$o$- and -$p$-, prep., 1574.
Poly-$p$-xylylene and related polymers, prep., 1604.
**D-Xylose,** 4-$O$-$\beta$-D-xylopyranosyl- and 3-$O$-methyl-4-$O$-($\beta$-D-xylopyranosyl)-, prep., 3674.

Z

**Zinc:** Dichloro(ethylenediamine)zinc, infrared spectrum and structure, 477.

# COMMUNICATIONS TO PROCEEDINGS: INDEX OF AUTHORS, 1961

The following index relates to Scientific Communications published in *Proceedings of The Chemical Society*, 1961.


A

**Abdus Sattar**, A. B. M. See **Henmo**, E., 238.
**Acheson**, R. M., **Hands**, A. R., and **Vernon**, J. M. New type of addition to 1-alkylpyrroles, 164.
**Adams**, D. M. Infrared-active metal–chlorine stretching frequencies, 335.
**Adams**, D. M. Solvent effects on the infrared spectra of inorganic complex hydrides, 431.
**Addison**, C. C., **Kilner**, M., and **Wojcicki**, A. Nitratopentacarbonylmanganese(I), 202
**Addison**, C. C., and **Walker**, A. Basic beryllium nitrate, 242.
**Addison**, C. C., **Johnson**, B. F. G., **Logan**, N., and **Wojcicki**, A. Transition-metal nitrites, 306.
**Adley**, T. J., and **Owen**, L. N. Thio-sugars with sulphur in the ring, 418.
**Ahmad**, A. See **Spenser**, I. D., 375.
**Alleston**, D. L., **Davies**, A. G., and **Figgis**, B. N. Structure of intermediates in the hydrolysis of dialkyltin(IV) compounds, 457.
**Apšimon**, J., and **Edwards**, O. E. Hetero-ring of diterpenoid alkaloids, 461.
**Arigoni**, D. See **Gopinath**, K. W., 446.
**Arison**, B. H. See **Trenner**, N. R., 214.
**Armarego**, W. L. F. Synthesis of three new triazanaphthalenes, 459.
**Arnold**, J., **Bertie**, J. E., and **Millen**, D. J. Infrared detection of hydrogen bonding in gaseous mixtures: the origin of broad bands, 121.
**Austin**, M. J., and **Parsons**, R. Anodic capacity of a mercury electrode in aqueous sodium fluoride solutions, 239.
**Ayres**, D. C., and **Pauwels**, P. J. S. Stereospecificity of lithium aluminium hydride reductions: reduction of podophyllotoxin, 388.
**Ayrey**, G., **Buncel**, E., and **Bourns**, A. N. Ylide mechanism in Hofmann elimination, 458.
**Ayscough**, P. B., **McCann**, A. P., and **Wilson**, R. The electron-spin resonance spectrum of triphenylmethyl, 16.
**Ayscough**, P. B., **Ivin**, K. J., and **O'Donnell**, J. H. Electron-spin resonance investigation of trapped hydrocarbon–sulphonyl radicals, 71.
**Ayscough**, P. B., **Cocker**, A. J., **Dainton**, F. S., **Hirst**, S., and **Weston**, M. Excited chloroethyl radicals $C_2H_xCl_{5-x}$, 244.
**Ayscough**, P. B., and **Thomson**, C. Electron-spin resonance spectra of alkyl radicals in $\gamma$-irradiated alkyl halides, 247.

B

**Baddeley**, G., **Baylis**, E. K., **Heaton**, B. G., and **Rasburn**, J. W. Reactions of 10-acetyl-1α-halogeno-*trans*-decalin: evidence for an unusual neighbouring-group effect, 451.
**Baddeley**, G., and **Khayat**, M. A. R. Hofmann *versus* Saytzeff elimination in the interaction of t-pentyl chloride and acetyl chloride, 382.
**Baddiley**, J. See **Frank**, W., 449.
**Bärnighausen**, H., **Jellinck**, F., and **Vos**, A. Structure of a sydnone, 120.
**Baird**, B. M., **Halsall**, T. G., **Jones**, E. R. H., and **Lowe**, G. Cephalosporin $P_1$, 257.
**Baldeschweiler**, J. D., and **Randall**, E. W. Measurement of chemical shifts by nuclear magnetic double resonance, 303.
**Ball**, W. J., and **Landor**, S. R. Synthesis of cyclic allenes, 143.
**Ball**, W. J., and **Landor**, S. R. Addition of carbenes to allenes, 245.
**Banks**, R. E., **Haszeldine**, R. N., and **McCreath**, M. K. Perfluoroalkylnitroso-compounds from perfluoroacyl nitrites, 64.
**Barclay**, G. A., **Harris**, C. M., **Hoskins**, B. F., and **Kokot**, E. Anomalous magnetic behaviour and binuclear structure of some so-called trico-ordinated copper(II) complexes, 264.
**Barfield**, P. A., **Lappert**, M. F., and **Lee**, J. $\pi$-Bonding and hindered rotation in inorganic systems, 421.
**Barker**, N. T., **Harris**, C. M., and **McKenzie**, E. D. Perchlorate co-ordination in metal complexes, 335.
**Barrow**, R. F. See **Robertson**, E. W., 329.
**Barton**, D. H. R., **Cheung**, H. T., **Cross**, A. D., **Jackman**, L. M., and **Martin-Smith**, M. Constitution of clerodin, 76.
**Barton**, D. H. R., and **Gupta**, G. S. Constitution of zierone, 308.
**Barton**, D. H. R., **Kirby**, G. W., **Taylor**, J. B., and **Thomas**, G. M. Biosynthesis of *Amaryllidaceae* alkaloids, 254.
**Barton**, D. H. R., and **Morgan**, L. R., jun. Synthesis of conessine, 206.
**Barton**, D. H. R. See **Gnoj**, O., 207.
**Battersby**, A. R., **Binks**, R., **Breuer**, S. W., **Fales**, H. M., and **Wildman**, W. C. Biosynthesis in the *Amaryllidaceae* incorporation of norbelladine into lycorine and norpluvine, 243.
**Battersby**, A. R., **Hodson**, H. F., **Rao**, G. V., and **Yeowell**, D. A. Alkaloids of calabash curare: caracurine-II and C-alkaloid D, 412.
**Battersby**, A. R., and **Yeowell**, D. A. Alkaloids of calabash curare: the structure of macusine-B, 17.
**Battersby**, A. R., **Yeowell**, D. A., **Jackman**, L. M., **Schroeder**, H.-D., **Hesse**, M., **Hiltebrand**, H., **von Philipsborn**, W., **Schmid**, H., and **Karrer**, P. Alkaloids of calabash curare: the structure of caracurine-II and C-alkaloid D, 413.
**Battersby**, A. R. See **McPhail**, A. T., 223.
**Baylis**, E. K. See **Baddeley**, G., 451.
**Bennett**, J. E. Detection of the phenalenyl radical in pyrolysed hydrocarbons by electron-spin resonance, 144.
**Bentley**, R., and **Keil**, J. G. Rôle of acetate and malonate in the biosynthesis of penicillic acid, 111.
**Berkoff**, C. E., **Cookson**, R. C., **Hudec**, J., and **Williams**, R. O. Dewar structures as intermediates in the synthesis of benzene derivatives, 312.
**Bertie**, J. E. See **Arnold**, J., 121.
**Beyerman**, H. C., and **Bontekoe**, J. S. t-Butoxy-group, a novel hydroxyl-protecting group for use in peptide synthesis with hydroxy-amino-acids, 249.
**Binks**, R. See **Battersby**, A. R., 243.
**Birch**, A. J., **Hodson**, H., **Moore**, B., and **Smith**, G. F. The reactions of echitamine, 62.
**Blomquist**, A. T., and **Maitlis**, P. M., 3,4-Dimethylenecyclobutene, 332.
**Blues**, E. T., and **Bryce-Smith**, D. Use of magnesium compounds in some new procedures for the alkylation of aromatic hydrocarbons, 245.
**Bolton**, J. R., and **Carrington**, A. Electron-spin resonance spectrum of the *p*-xylene positive ion, 174.
**Bolton**, J. R., and **Carrington**, A. Electron-spin resonance spectra of semiquinones in sulphuric acid: a reassignment of spectra previously attributed to the *p*-xylene positive ion, 385.
**Bonner**, W. A. See **Meyer zu Reckendorf**, W., 429.
**Bonnett**, R., and **White**, J. D. Reductive condensation of 2,5-dimethylpyrrole: a novel isoindoline synthesis, 119.

**Bontekoe, J. S.** See **Beyerman, H. C.**, 249.
**Booth, G.**, and **Chatt, J.** Carbonylation of platinum and palladium organo-complexes, 67.
**Bourns, A. N.** See **Ayrey, G.**, 458.
**Breuer, S. W.** See **Battersby, A. R.**, 243.
**Brivati, J. A.**, **Hulme, R.**, and **Symons, M. C. R.** Hyperfine interactions from methyl groups in aromatic positive ions, 384.
**Brivati, J. A.**, **Keen, N.**, **Symons, M. C. R.**, and **Trevalian, P. A.** Radicals in irradiated formates and oxalates, 66.
**Brown, R. D.**, and **Harcourt, R. D.** $\sigma$-Electron delocalisation and the electronic structure of dinitrogen tetroxide, 216.
**Brown, J. K.**, and **Tyler, J. K.** The infrared spectra of monofluoro- and monoiodo-acetylene, 13.
**Brown, W. A. C.**, **Trotter, J.**, and **Robertson, J. M.** *X*-Ray study of crystals isolated during the synthesis of 1,12-*o*-phenyleneperylene, 115.
**Brownlee, T. H.**, and **Saunders, W. H., jun.** Orientation in some elimination reactions in cyclic systems, 314.
**Brueckner, D. A.**, **Hamor, T. A.**, **Robertson, J. M.**, and **Sim, G. A.** Stereochemistry of (−)-2-bromo-2-nitrocamphane, 306.
**Bryan, R. F.**, and **Knopf, P. M.** Crystal structure of primary cupric dithizonate, 203.
**Bryce-Smith, D.**, and **Lodge, J. E.** Preparation of cyclo-octatetraenes by the photo-addition of acetylenes to benzene, 333.
**Bryce-Smith, D.** See **Blues, E. T.**, 245.
**Bullen, G. J.** See **Gee, W.**, 432.
**Bu'Lock, J. D.**, and **Smalley, H. M.** Biosynthesis of aromatic substances from acetyl- and malonyl-coenzyme A, 209.
**Buncel, E.** See **Ayrey, G.**, 458.
**Bunnett, J. F.**, **Hauser, C. F.**, and **Nahabedian, K. V.** Relative thermodynamic affinities of hydroxide and thiophenoxide ions for carbon, 305.
**Burg, A. B.** See **Griffiths, J. E.**, 12.

C

**Carrington, A.** See **Bolton, J. R.**, 174, 385.
**Challis, B. C.**, and **Ridd, J. H.** Mechanisms of diazotisation at intermediate acidities, 173.
**Chambers, R. D.**, **Musgrave, W. K. R.**, and **Savory, J.** Addition of "Halogen monofluorides" to fluoro-olefins, 113.
**Chapman, D.**, **Golding, R. M.**, **Massey, A. G.**, and **Moelwyn-Hughes, J. T.** Electron-spin resonance spectra of sulphur nitride ions, 377.
**Chatt, J.** See **Booth, G.**, 67.
**Cheung, H. T.** See **Barton, D. H. R.**, 76.
**Chiang, Y.** See **Kresge, A. J.**, 81.
**Clark-Lewis, J. W.**, and **Jackman, L. M.** Stereochemistry and conformation of flavan derivatives, 165.
**Clemo, G. R.**, and **Raper, R.** Molecular dissymmetry due to symmetrically placed hydrogen and deuterium, 333.
**Coates, G. E.**, and **Green, S. I. E.** Coloured bipyridyl complexes of beryllium, 376.
**Cocker, A. J.** See **Ayscough, P. B.**, 244.
**Cohen, S. G.**, **Orman, S.**, and **Laufer, D.** Chain-inhibition of a non-chain reaction, 301.
**Cookson, R. C.**, **Hudec, J.**, and **Whitear, B.** Cyclopentadienide anion that is stable in water, 117.
**Cookson, R. C.**, and **MacKenzie, S.** Intensification of absorption and rotation of the carbonyl chromophore by mixing of $n \longrightarrow \pi^*$ with $\pi \longrightarrow \pi^*$ transitions, 423.
**Cookson, R. C.** See **Berkoff, C. E.**, 312.
**Corbett, G. E.**, and **Williams, G. H.** Homolytic aromatic methylation, 240.
**Cottrell, T. L.**, and **Matheson, A. J.** Measurement of the vibrational relaxation time of tetradeuteromethane, 114.
**Cowie, G. R.**, **Fox, J. R.**, **Fitches, M. J. H.**, **Hooton, K. A.**, **Hunt, D. M.**, **Kohnstam, G.**, and **Shillaker, B.** Entropies and heat capacities of activation in solvolysis by $S_N$ mechanisms, 222.
**Crabtree, J. M.**, **Marsh, D. W.**, **Tomkinson, J. C.**, **Williams, R. J. P.**, and **Fernelius, W. C.** Stability constants of some complexes of the early cations of the first transition series, 336.
**Craig, D. P.**, and **Thirunamachandran, T.** Intermolecular interactions in mixed crystals, 253.
**Crenshaw, R. R.**, and **Owen, T. C.** Structure of thiosulphonates; a chemical distinction between thiosulphonate and disulphoxide formulations, 250.
**Crombie, L.**, **Godin, P. J.**, **Siddalingaiah, K. S.**, and **Whiting, D. A.** Rotenoid reactions prefaced by alkaline attack, 19.
**Crombie, L.**, and **Lown, J. W.** Determination of the geometry of the B/C fusion of rotenoids by means of long-range asymmetric magnetic shielding of the carbonyl group, 299.
**Cromwell, N. H.** See **Kevill, D. N.**, 252.
**Cross, A. D.** See **Barton, D. H. R.**, 76.

D

**Dainton, F. S.** See **Ayscough, P. B.**, 244.
**Das, S. N.**, and **Ives, D. J. G.** Hydrogen bonding in the acid malonate ion, 373.
**Davies, A. G.**, **Hare, D. G.**, **Khan, O. R.**, and **Sikora, J.** Monomethylenation and polymethylenation by diazomethane in the presence of boron compounds, 172.
**Davies, A. G.**, and **Smith, W. MacF.** Rates of association of thiocyanate ions with nickel(II) and cobalt(II) ions, 380.
**Davies, A. G.** See **Alleston, D. L.**, 457.
**Davis, B. T.**, **Halsall, T. G.**, and **Hands, A. R.** Reduction of ascaridole with ferrous sulphate solution, 83.
**Davis, J. B.**, **Jackman, L. M.**, **Siddons, P. T.**, and **Weedon, B. C. L.** Structures of phytoene, phytofluene, $\zeta$-carotene, and neurosporene, 261.
**de Mayo, P.** See **Henmo, E.**, 238.
**Dent, W. T.**, **Duncanson, L. A.**, **Guy, R. G.**, **Reed, H. W. B.**, and **Shaw, B. L.** Synthesis and structure of complexes of the type $[Co_3(CO)_9(CY)]$, 169.
**Deulofeu, V.** See **Robinson, B.**, 310.
**Dewar, J. H.** See **Shaw, G.**, 216.
**Djerassi, C.**, **Murray, R. D. H.**, and **Villotti, R.** Structure of the cactus sterol, peniocerol (cholest-8-ene-3$\beta$,6$\alpha$-diol), 450.
**Drake, J. E.**, and **Jolly, W. L.** Preparation and identification of volatile germanes, 379.
**Duncanson, L. A.** See **Dent, W. T.**, 169.
**Dunitz, J. D.** See **Huber-Buser, E.**, 463.

E

**Edwards, O. E.** See **ApSimon, J.**, 461.
**Elliott, M.**, and **Jeffs, K. A.** Synthesis of calythrone, 376.
**Etter, R. M.** See **Skell, P. S.**, 443.
**Evans, A. G.**, **Evans, J. C.**, and **Owen, E. D.** Catalytic action of anionic catalysts, 339.
**Evans, D. F.** See **Maher, J. P.**, 208.
**Evans, J. C.** See **Evans, A. G.**, 339.
**Everard, A. F.**, and **Swan, G. A.** Free-radical arylation and aroylation of aromatic compounds induced by gamma-radiation, 212.

F

**Fales, H. M.** See **Battersby, A. R.**, 243.
**Falshaw, C. P.**, **Johnson, A. W.**, and **King, T. J.** Pyrolytic decomposition of maytenone: a model system, 265.
**Farrell, P. G.**, and **Mason, S. F.** Electronic spectra of alkyl and double-bond carbonium ions, 256.
**Feeney, J.**, and **Sutcliffe, L. H.** Nuclear magnetic resonance study of hydrogen bonding in liquid amines, 118.
**Ferguson, G.**, and **Sim, G. A.** Steric effects in substituted benzoic acids, 162.
**Fernelius, W. C.** See **Crabtree, J. M.**, 336.
**Figgis, B. N.** See **Alleston, D. L.**, 457.
**Firth, J. G.** See **Tyrell, H. J. V.**, 201.
**Fischer, A.**, **Packer, J.**, **Vaughan, J.**, and **Wright, G. J.** Acetoxylation accompanying nitration with nitric acid–acetic anhydride mixtures, 369.
**Fitches, M. J. H.** See **Cowie, G. R.**, 222.
**Fitzsimmons, B. W.**, and **Shaw, R. A.** Rearrangement of some alkoxyphosphazenes, 258.

**Fletcher,** J. M. See **Scargill,** D., 251.
**Fleming,** I., and **Harley-Mason,** J. New synthesis of acetylenic bonds and its biosynthetic implications, 245.
**Fox,** J. R. See **Cowie,** G. R., 222.
**Frank,** W., **Wieczorkowski,** J., **Hughes,** N. A., and **Baddiley,** J. Alkali hydrolysis of sulphonium nucleosides, 449.
**Frydman,** B. See **Robinson,** B., 310.

G

**Gee,** W., **Shaw,** R. A., **Smith,** B. C., and **Bullen,** G. J. Dimeric phosphinoborine derivatives, 432.
**Gerrard,** W., and **Hudson,** H. R. Hydrogen dichloride, $HCl_2^-$, ion as a reagent in alcohol–hydrogen chloride systems, 467.
**Gil-Av,** E., and **Herzberg-Minzly,** Y. Gas-chromatographic study of the rate of Diels–Alder addition, 316.
**Gillespie,** R. J., **Oubridge,** J. V., and **Robinson,** E. A. Polysulphuryl fluorides, 427.
**Glasel,** J. A., **Jackman,** L. M., and **Turner,** D. W. Spin decoupling and relative chemical shifts of dissimilar nuclei measured by using frequency related oscillators, 426.
**Gnoj,** O., **Oliveto,** E. P., **Robinson,** C. H., and **Barton,** D. H. R. Preparation of 5,9-cyclosteroids, 207.
**Godfrey,** M., and **Murrell,** J. N. Nature of the first absorption band of nitrobenzene, 171.
**Godin,** P. J., and **Thain,** E. M. Biosynthesis of chrysanthemum-monocarboxylic acid, 452.
**Godin,** P. J. See **Crombie,** L., 19.
**Gold,** V. $H_0$ Function and general acid catalysis in aromatic hydrogen exchange and other proton transfer reactions, 453.
**Golding,** R. M. See **Chapman,** D., 377.
**Gopinath,** K. W., **Govindachari,** T. R., **Parthasarathy,** P. G., **Viswanathan,** N., **Arigoni,** D., and **Wildman,** W. C. Structure of cedrelone, 446.
**Gough,** S. T. D., and **Trippett,** S. New synthesis of acetylenes, 302.
**Govindachari,** T. R. See **Gopinath,** K. W., 446.
**Grant,** I. G., **Hamilton,** J. A., **Hamor,** T. A., **Hodges,** R., **McGeachin,** S. G., **Raphael,** R. A., **Robertson,** J. M., and **Sim,** G. A. Structure of cedrelone, 444.
**Grdenić,** D., and **Kamenar,** B. Structures involving unshared electron pair; pyramidal configuration of trichlorostannite ion, 304.
**Green,** M., and **Hudson,** R. F. Optical resolution of ethylphenylphosphinothiolic acid, 145.
**Green,** M. L. H., and **Nagy,** P. An unusual protonation reaction of some $\sigma$-bonded allyl complexes, 378.
**Green,** S. I. E. See **Coates,** G. E., 376.
**Griffiths,** J. E., and **Burg,** A. B. An anti-Arbuzov rearrangement, 12.
**Griffiths,** J. E., and **McAfee,** K. B. Microwave spectrum of germyl fluoride, 456.
**Grinter,** R., and **Mason,** S. F. Electronic spectra of arylmethyl ions, 386.
**Groth,** P., and **Hassel,** O. Charge-transfer bonds in solids: crystal structure of oxalyl bromide, 343.
**Gupta,** G. S. See **Barton,** D. H. R., 308.
**Guy,** R. G. See **Dent,** W. T., 169.

H

**Haber,** J., and **Stone,** F. S. Crystal field stabilisation as a factor in surface processes, 424.
**Habib,** M. S., and **Rees,** C. W. Rearrangement of certain quinoxalinecarboxyanilides. Isolation of an intermediate in a related *N*-oxide rearrangement, 167.
**Halsall,** T. G. See **Baird,** B. M., 257; **Davis,** B. T., 83.
**Hamilton,** J. A., **Hamor,** T. A., **Robertson,** J. M., and **Sim,** G. A. The structure of echitamine, 63.
**Hamilton,** J. A. See **Grant,** I. G., 444.
**Hamor,** T. A. See **Brueckner,** D. A., 306; **Grant,** I. G., 444; **Hamilton,** J. A., 63; **Sim,** G. A., 75.
**Hands,** A. R. See **Acheson,** R. M., 164; **Davis,** B. T., 83.
**Harcourt,** R. D. See **Brown,** R. D., 216.
**Hare,** D. G. See **Davies,** A. G., 172.
**Hargreaves,** A., **Rizvi,** S. H., and **Trotter,** J. Structure of crystalline biphenyl, 122.
**Harley-Mason,** J. See **Fleming,** I., 245.
**Harris,** C. M. See **Barclay,** G. A., 264; **Barker,** N. T., 335.
**Harris,** G. S. The nature of tertiary arsine–halogen adducts, 65.
**Harris,** R. K., and **Sheppard,** N. Ring inversion in cyclohexane and related molecules as studied by nuclear magnetic resonance, 418.
**Hassel,** O. See **Groth,** P., 343.
**Hasseldine,** R. N. See **Banks,** R. E., 64.
**Hauser,** C. F. See **Bunnett,** J. F., 305.
**Heaton,** B. G. See **Baddeley,** G., 451.
**Hemmerich,** P. See **Rowan,** T., 260.
**Henmo,** E., **de Mayo,** P., **Abdus Sattar,** A. B. M., and **Stoessel,** A. Irradiation of unsaturated sultones, 238.
**Herzberg-Minzly,** Y. See **Gil-Av,** E., 316.
**Hesse,** M. See **Battersby,** A. R., 413.
**Higginson,** W. C. E. See **Nyburg,** S. C., 297.
**Hiltebrand,** H. See **Battersby,** A. R., 413.
**Hirst,** D. M., and **Linnett,** J. W. New method for deriving molecular wave functions, 427.
**Hirst,** S. See **Ayscough,** P. B., 244.
**Hodges,** R. See **Grant,** I. G., 444.
**Hodson,** H. See **Birch,** A. J., 62.
**Hodson,** H. F., **Robinson,** B., and **Smith,** G. F. Chimonanthine, a new calycanthaceous alkaloid, 465.
**Hodson,** H. F. See **Battersby,** A. R., 412; **McPhail,** A. T., 223.
**Hojo,** M. See **Ledwith,** A., 241.
**Holliday,** A. K., **Peach,** M. E., and **Waddington,** T. C. Hexachlorodiborate anion, $B_2Cl_6^{2-}$, 220.
**Holker,** J. S. E., and **Whalley,** W. B. Conformation of ring A in some 4,4-dimethyl-steroid and triterpenoid 3-ketones, 464.
**Homer,** J., and **Thomas,** L. F. Nuclear magnetic resonance spectra of *cis*- and *trans*-perfluorodecalin, 139.
**Hooton,** K. A. See **Cowie,** G. R., 222.
**Hoskins,** B. F. See **Barclay,** G. A., 264.
**Huber-Buser,** E., **Dunitz,** J. D., and **Venkatesan,** K. Conformation of the cyclodecane ring, 463.
**Hudec,** J. See **Berkoff,** C. E., 312; **Cookson,** R. C., 117.
**Hudson,** H. R. See **Gerrard,** W., 467.
**Hudson,** R. F. See **Green,** M., 145.
**Hughes,** N. A. See **Frank,** W., 449.
**Hulme,** R. See **Brivati,** J. A., 384.
**Hunt,** D. M. See **Cowie,** G. R., 222.
**Hunt,** G. R., and **Ross,** I. G. Electronic excitation in azulene, 11.
**Hurst,** J. J., and **Whitham,** G. H. Photoisomerisation of eucarvone to 1,5,5-trimethylnorborn-2-en-7-one, 116.

**Ives,** D. J. G. See **Das,** S. N., 373.
**Ivin,** K. J. See **Ayscough,** P. B., 71.

J

**Jackman,** L. M. See **Barton,** D. H. R., 76; **Battersby,** A. R., 413; **Clark-Lewis,** J. W., 165; **Davis,** J. B., 261; **Glasel,** J. A., 426.
**Jackson,** A. H. See **Smith,** G. F., 310.
**James,** D. G. L., and **MacCallum,** D. Kinetic study of the addition of the ethyl radical to vinyl monomer, 259.
**Jeffs,** K. A. See **Elliott,** M., 376.
**Jellinck,** F. See **Bärnighausen,** H., 120.
**Johnson,** A. W., and **Kay,** I. T. Synthesis of derivatives of corrole. An amendment, 168.
**Johnson,** A. W., and **Shaw,** N. Isolation of a crystalline nucleoside from the vitamin $B_{12}$ co-enzyme, 447.
**Johnson,** A. W. See **Falshaw,** C. P., 265.
**Johnson,** B. F. G. See **Addison,** C. C., 306.
**Jolly,** W. L. See **Drake,** J. E., 379.
**Jones,** A. S., and **Parsons,** D. G. Fractionation of ribonucleic acids by means of a new type of exchanger, 78.
**Jones,** E. R. H. See **Baird,** B. M., 257.

**Jones**, R. A. Y. See **Moynehan**, T. M., 218.
**Jones**, W. J., and **Sheppard**, N. Internal rotation of methyl groups as detected by bond contours in infrared spectra of solutions and gases, 420.

K

**Kamenar**, B. See **Grdenić**, D., 304.
**Karrer**, P. See **Battersby**, A. R., 413.
**Katritzky**, A. R., and **Øksne**, S. Reaction of β-keto-esters with hydroxylamine, 387.
**Katritzky**, A. R. See **Moynehan**, T. M., 218.
**Kay**, I. T. See **Johnson**, A. W., 168.
**Keen**, N. See **Brivati**, J. A., 66.
**Keil**, J. G. See **Bentley**, R., 111.
**Kevill**, D. N., and **Cromwell**, N. H. Mechanism of merged substitution and elimination, 252.
**Khan**, O. R. See **Davies**, A. G., 172.
**Khayat**, M. A. R. See **Baddeley**, G., 382.
**Kiang**, A. K., **Lee**, H. H., and **Sim**, K. Y. Structures of linderone and methyl-linderone, 455.
**Kilner**, M. See **Addison**, C. C., 202.
**King**, R. B., **Treichel**, P. M., and **Stone**, F. G. A. Fluorocarbon derivatives of the metal carbonyls, 69.
**King**, T. J. See **Falshaw**, C. P., 265.
**Kirby**, G. W. See **Barton**, D. H. R., 254.
**Kirk**, D. N., and **Petrow**, V. New route to 4-methyl-3-oxo-$\Delta^4$-steroids, 114.
**Klanberg**, F. Complex pseudohalides of boron and aluminium, 203.
**Knopf**, P. M. See **Bryan**, R. F., 203.
**Knowles**, J. R., **Norman**, R. O. C., and **Prosser**, J. H. Transition state in nucleophilic aromatic substitution, 341.
**Kohnstam**, R. See **Cowie**, G. R., 222.
**Kokot**, E. See **Barclay**, G. A., 264.
**Kouwenhoven**, H. W., **Lewis**, J., and **Nyholm**, R. S. Complexes involving an olefinic tertiary arsine chelate group, 220.
**Kresge**, A. J., and **Chiang**, Y. Kinetics and equilibria of 1,3,5-trimethoxybenzene in concentrated aqueous acid, 81.

L

**Landor**, S. R. See **Ball**, W. J., 143, 245.
**Lappert**, M. F., and **Majumdar**, M. K. Unsymmetrically substituted borazoles and some bicyclic derivatives thereof, 425.
**Lappert**, M. F. See **Barfield**, P. A., 421.
**Laufer**, D. See **Cohen**, S. G., 301.
**Ledwith**, A., **Hojo**, M., and **Winston**, S. Racemisation and radio-chloride exchange of *p*-chlorobenzhydryl chloride with mercuric chloride, 241.
**Lee**, H. H. See **Kiang**, A. K., 455.
**Lee**, J. See **Barfield**, P. A. 421.
**Leffler**, J. E., and **Ramsey**, B. G. End groups in the polymer from the reaction of diazomethane with organoboron compounds, 117.
**Legge**, N., and **Pullin**, A. D. E. Partial resolution of the rotational structure of a bending vibration of thiocyanic acid in solution, 342.
**Lewis**, J. See **Kouwenhoven**, H. W., 220.
**Linnett**, J. W. See **Hirst**, D. M., 427.
**Lloyd**, D. R., and **Prince**, R. H. Hydrogen malonate ion, 464.
**Lodge**, J. E. See **Bryce-Smith**, D., 333.
**Logan**, N. See **Addison**, C. C., 306.
**Lowe**, G. See **Baird**, B. M., 257.
**Lown**, J. W. See **Crombie**, L., 299.
**Luxmoore**, A. R., and **Truter**, M. R. Crystal structure of tetracarbonylacrylonitrileiron, 466.

M

**McAlee**, K. B. See **Griffiths**, J. E., 456.
**McCann**, A. P. See **Ayscough**, P. B., 16.
**McCorkindale**, N. J., and **Sime**, J. G. Configuration of fumagillin, 331.
**McCreath**, M. K. See **Banks**, R. E., 64.
**McCrindle**, R., **Overton**, K. H., and **Raphael**, R. A. Catalytic hydrogenation of succinic anhydrides, 313.
**MacCallum**, D. See **James**, D. G. L., 259.
**McGarth**, B. P., and **Tedder**, J. M. Mechanism of allylic bromination by *N*-bromosuccinimide, 80, 199.
**McGeachin**, S. G. See **Grant**, I. G., 444.
**McKenzie**, E. D. See **Barker**, N. T., 335; **Cookson**, R. C., 423.
**McPhail**, A. T., **Robertson**, J. M., **Sim**, G. A., **Battersby**, A. R., **Hodson**, H. F., and **Yeowell**, D. A. Alkaloids of calabash curare: the structure of mascusine-A, 223.
**McPhail**, A. T., and **Sim**, G. A. Structure of caracurine-II, 416.
**Maher**, J. P., and **Evans**, D. F. Proton magnetic resonance spectra of thallium trialkyls; chemical exchange and formation of mixed alkyls, 208.
**Mair**, G. A., **Powell**, H. M., and **Venanzi**, L. M. Stereochemistry of a five-co-ordinated platinum compound, 170.
**Maitlis**, P. M. See **Blomquist**, A. T., 332.
**Majumdar**, M. K. See **Lappert**, M. F., 425.
**Mak**, T. C. W., and **Trotter**, J. Structure of biphenylene, 163.
**Marsh**, D. W. See **Crabtree**, J. M., 336.
**Martin**, D. F. See **Randall**, W. J., 340.
**Martin**, D. L., and **Rossotti**, F. J. C. The structure of dimeric acetic acid in aqueous solution, 73.
**Martin-Smith**, M. See **Barton**, D. H. R., 76.
**Mason**, S. F. See **Farrell**, P. G., 256; **Grinter**, R., 386.
**Massey**, A. G. See **Chapman**, D., 377.
**Matheson**, A. J. See **Cottrell**, T. L., 114.
**Meyer zu Reckendorf**, W., and **Bonner**, W. A. Sulphur substitution compounds of amino-sugars. Part III, 429.
**Millen**, D. J. See **Arnold**, J., 121.
**Moeller**, T. See **Randall**, W. J., 340.
**Moelwyn-Hughes**, J. T. See **Chapman**, D., 377.
**Moore**, B. See **Birch**, A. J., 62.
**Morgan**, L. R., jun. See **Barton**, D. H. R., 206.
**Moynehan**, T. M., **Schofield**, K., **Jones**, R. A. Y., and **Katritzky**, A. R. Quinolizidine stereochemistry, 218.
**Mulloy**, J. A. See **O'Colla**, P. S., 300.
**Murray**, R. D. H. See **Djerassi**, C., 450.
**Murrell**, J. N. See **Godfrey**, M., 171.
**Musgrave**, W. K. R. See **Chambers**, R. D., 113.

N

**Nagy**, P. See **Green**, M. L. H., 378.
**Nahabedian**, K. V. See **Bunnett**, J. F., 305.
**Nelson**, S. M. Tetrahedral and bridged octahedral complexes of cobalt(II), 372.
**Niccolini**, M. See **Turco**, A., 213.
**Nonhebel**, D. C. Reactions of cupric halides with aromatic hydrocarbons, 307.
**Norman**, R. O. C. See **Knowles**, J. R., 341.
**Nyburg**, S. C., **Wood**, J. S., and **Higginson**, W. C. E. Solution spectra and crystal spectra of Lifschitz nickel(II) complexes, 297.
**Nyholm**, R. S. See **Kouwenhoven**, H. W., 220.

O

**O'Colla**, P. S., **O'Donnell**, J. J., and **Mulloy**, J. A. Application of the Weerman reaction to polysaccharides, 300.
**O'Donnell**, J. H. See **Ayscough**, P. B., 71.
**O'Donnell**, J. J. See **O'Colla**, P. S., 300.
**Okawara**, R. Dimerisation, by co-ordination, of distannoxanes, 383.
**Oliveto**, E. P. See **Gnoj**, O., 207.
**Onyszchuk**, M. See **Srivastava**, T. N., 205.
**Openshaw**, H. T., and **Whittaker**, N. Reaction of methoxycarbonylmethylenetriphenylphosphorane with hindered ketones, 454.
**Orman**, S. See **Cohen**, S. G., 301.
**Oubridge**, J. V. See **Gillespie**, R. J., 427.
**Overton**, K. H., **Weir**, N. G., and **Wylie**, A. Stereochemistry of columbin, 211.

**Overton**, K. H. See **McCrindle**, R., 313.
**Owen**, E. D. See **Evans**, A. G., 339.
**Owen**, L. N. See **Adley**, T. J., 418.
**Owen**, T. C. See **Crenshaw**, R. R., 250.
**Øksne**, S. See **Katritzky**, A. R., 387.

P

**Packer**, J. See **Fischer**, A., 369.
**Parker**, A. J. Carbon-basicity of halide and halogenoid ions in nitrobenzene, 371.
**Parker**, W., **Ramage**, R., and **Raphael**, R. A. Synthesis of (±)-cuparene, 74.
**Parsons**, D. G. See **Jones**, A. S., 78.
**Parsons**, R. See **Austin**, M. J., 239.
**Parthasarathy**, P. C. See **Gopinath**, K. W., 446.
**Paterson**, W., and **Proctor**, G. R. Novel elimination reaction, 248.
**Patrick**, C. R. See **Smith**, B. J. K., 138.
**Paul**, I. C. See **Sim**, G. A., 75.
**Pauwels**, P. J. S. See **Ayres**, D. C., 388.
**Peach**, M. E. See **Holliday**, A. K., 220.
**Pecile**, C. See **Turco**, A., 213.
**Pelletier**, S. W. See **Solo**, A. J., 14.
**Penfold**, J., and **Plesch**, P. H. Chain-transfer by anisole in the cationic polymerisation of isobutene, 311.
**Pepper**, D. C., and **Reilly**, P. J. Polymerisation of styrene by perchloric acid, 200.
**Pepper**, D. C., and **Reilly**, P. J. Transfer mechanisms in the cationic polymerisation of styrene, 460.
**Petrow**, V. See **Kirk**, D. N., 114.
**Phillips**, L. Addition of methyl radicals to nitrosomethane in the vapour phase: trimethylhydroxylamine, 204.
**Phillips**, L. Abstraction of chlorine atoms from gaseous t-butyl hypochlorite by methyl radicals, 338.
**Pink**, R. C. See **Rooney**, J. J., 70, 142.
**Plesch**, P. H. See **Penfold**, J., 311.
**Pocker**, Y. Optical resolution of $C_6H_5{\cdot}CH(OH){\cdot}C_6D_5$ and $C_6H_5{\cdot}CD(OH){\cdot}C_6D_5$. Preparation and racemisation of (−)-$C_6H_5{\cdot}CHCl{\cdot}C_6D_5$ and (−)-$C_6H_5{\cdot}CDCl{\cdot}C_6D_5$, 140.
**Pocker**, Y. Mechanism of the gas-phase Claisen rearrangement of allyl vinyl ethers, 141.
**Powell**, H. M. See **Mair**, G. A., 170.
**Praill**, P. F. G., and **Whitear**, A. L. Acid-catalysed self-condensation of acetic anhydride and analogous compounds, 112.
**Prince**, R. H. See **Lloyd**, D. R., 464.
**Proctor**, G. R. See **Paterson**, W., 248.
**Prosser**, J. H. See **Knowles**, J. R., 341.
**Pullin**, A. D. E. See **Legge**, N., 342.

R

**Ramage**, R. See **Parker**, W., 74.
**Ramsey**, B. G. See **Leffler**, J. E., 117.
**Randall**, E. W. See **Baldeschweiler**, J. D., 303.
**Randall**, W. J., **Martin**, D. F., and **Moeller**, T. Application of high-speed digital computers to the calculation of formation constants for tervalent-metal complexes, 340.
**Rao**, G. V. See **Battersby**, A. R., 412.
**Raper**, R. See **Clemo**, G. R., 333.
**Raphael**, R. A. See **Grant**, I. G., 444; **McCrindle**, R., 313; **Parker**, W., 74.
**Rasburn**, J. W. See **Baddeley**, G., 451.
**Reed**, H. W. B. See **Dent**, W. T., 169.
**Rees**, C. W. See **Habib**, M. S., 167.
**Reilly**, P. J. See **Pepper**, D. C., 200, 460.
**Richardson**, A. C. Derivatives of 3-amino-3,6-dideoxy-L-glucose and -L-talose, 255.
**Richardson**, A. C. Synthesis and stereochemistry of mycaminose, 430.
**Ridd**, J. H. See **Challis**, B. C., 173.
**Rizvi**, S. H. See **Hargreaves**, A., 122.
**Robertson**, E. W., and **Barrow**, R. F. Rotational analysis of the $C^3\Pi_u$–$X^1\Sigma_g^+$ system of $K_2$, and ionisation potential of $K_2$, 329.
**Robertson**, J. M. See **Brown**, W. A. C., 115; **Brueckner**, D. A., 306; **Grant**, I. G., 444; **Hamilton**, J. A., 63; **McPhail**, A. T., 223; **Sim**, G. A., 75.
**Robinson**, B., **Smith**, G. F. Jackson, A. H. **Shaw**, D., **Frydman**, B., and **Deulofeu**, V. Dehydrobufotenin, 310.
**Robinson**, B. See **Hodson**, H. F., 465.
**Robinson**, C. H. See **Gnoj**, O., 207.
**Robinson**, E. A. See **Gillespie**, R. J., 427.
**Rooney**, J. J., and **Pink**, R. C. A study by electron-spin resonance of the adsorption of hydrocarbons on a silica–alumina catalyst, 70.
**Rooney**, J. J., and **Pink**, R. C. Interaction between aluminium chloride and aromatic hydrocarbons, 142.
**Ross**, I. G. See **Hunt**, G. R., 11.
**Rossotti**, F. J. C. See **Martin**, D. L., 73.
**Rowan**, T., **Wood**, H. C. S., and **Hemmerich**, P. Nucleophilic additions of 8-substituted pteridines and their biochemical significance, 260.
**Rusina**, A. See **Vlček**, A. A., 161.

S

**Saunders**, W. H., jun. See **Brownlee**, T. H., 314.
**Saville**, B. Thiourea as a leaving group from carbon in $S_N$ displacements, 214.
**Savory**, J. See **Musgrave**, W. K. R., 113.
**Scargill**, D., and **Fletcher**, J. M. Nitratonitrosylruthenium complexes, 251.
**Schmid**, H. See **Battersby**, A. R., 413.
**Schofield**, K. See **Moynehan**, T. M., 218.
**Schroeder**, H.-D. See **Battersby**, A. R., 413.
**Schwarz**, J. C. P., and **Yule**, K. C. D-Xylothiapyranose: a sugar with sulphur in the ring, 417.
**Sharpe**, L. H. Observations of molecular interactions in oriented monolayers by infrared spectroscopy involving total internal reflection, 461.
**Shaw**, B. L. See **Dent**, W. T., 169.
**Shaw**, D. See **Robinson**, B., 310.
**Shaw**, G., and **Dewar**, J. H. Synthesis of DL-willardine, 216.
**Shaw**, G., and **Wilson**, D. V. Synthesis of 5-amino-1-β-D-ribofuranosylimidazole-4-carboxylic acid 5′-*O*-phosphate, 381.
**Shaw**, N. See **Johnson**, A. W., 447.
**Shaw**, R. A. See **Fitzsimmons**, B. W., 258, **Gee**, W., 432.
**Sheppard**, N. See **Harris**, R. K., 418, **Jones**, W. J., 420.
**Shillacker**, B. See **Cowie**, G. R., 222.
**Sicher**, J. See **Zavada**, J., 199.
**Siddalingaiah**, K. S. See **Crombie**, L., 19.
**Siddons**, P. T. See **Davis**, J. B., 261.
**Sikora**, J. See **Davies**, A. G., 172.
**Sim**, G. A., **Hamor**, T. A., **Paul**, I. C., and **Robertson**, J. M. Structure of clerodin, 75.
**Sim**, G. A. See **Brueckner**, D. A., 306; **Ferguson**, G., 162; **Grant**, I. G., 444; **Hamilton**, J. A., 63; **McPhail**, A. T., 223, 416.
**Sim**, K. Y. See **Kiang**, A. K., 455.
**Sime**, J. G. See **McCorkindale**, N. J., 331.
**Skell**, P. S., and **Etter**, R. M. Steric discrimination in reactions of ethoxycarbonylcarbene: norcarane-7-carboxylic acid, 443.
**Smalley**, H. M. See **Bu'Lock**, J. D., 209.
**Smith**, B. C. See **Gee**, W. H., 432.
**Smith**, B. J. K., and **Patrick**, C. R. *cis*- and *trans*-Perfluorodecalin, 138.
**Smith**, G. F. See **Birch**, A. J., 62, **Hodson**, H. F., 465, **Robinson**, B., 310.
**Smith**, W. MacF. See **Davies**, A. G., 380.
**Solo**, H. J., and **Pelletier**, S. W. The stereochemistry of the E- and F-rings of atisine: its relation to the atisine–isoatisine isomerisation, 14.
**Spector**, M. L. See **Stern**, E. W., 370.
**Spenser**, I. D., and **Ahmad**, A. α-Amino-acids and α-keto acid oximes from α-hydroxyamino-acids: a new disproportionation reaction, 375.
**Srivastava**, T. N., and **Onyszchuk**, M. Mono- and di-fluorogermane, 205.
**Stern**, E. W., and **Spector**, M. L. Reaction of olefin–palladium(II) chloride complexes with nucleophiles: a new vinylation, 370.

**Stewart**, J. M., and **Weale**, K. E. Transition-state volume change in a reverse Menschutkin reaction, 389.
**Stoessel**, A. See **Henmo**, E., 238.
**Stone**, F. G. A. See **King**, R. B., 69.
**Stone**, F. S. See **Haber**, J., 424.
**Sutcliffe**, L. H. See **Feeney**, J., 118.
**Swallow**, A. G., and **Truter**, M. R. Structure of bipyridyl-(1-acetylacetonyl)trimethylplatinum(IV), 166.
**Swan**, G. A. See **Edward**, A. F., 212.
**Symons**, M. C. R. See **Brivati**, J. A., 66, 384.

T

**Taub**, D. See **Trenner**, N. R., 214.
**Taylor**, J. B. See **Barton**, D. H. R., 254.
**Tedder**, J. M. See **McGrath**, B. P., 80, 199.
**Thain**, E. M. See **Godin**, P. J., 452.
**Thirunamachandran**, T. See **Craig**, D. P., 253.
**Thomas**, G. M. See **Barton**, D. H. R., 254.
**Thomas**, L. F. See **Homer**, J., 139.
**Thomson**, C. See **Ayscough**, P. B., 247.
**Thynne**, J. C. J. Dimerisation and disproportionation of n-butyl radicals, 18.
**Thynne**, J. C. J. Reaction of ethyl radicals with isopropyl radicals, 68.
**Tomkinson**, J. C. See **Crabtree**, J. M., 336.
**Treichel**, P. M. See **King**, R. B., 69.
**Trenner**, N. R., **Arison**, B. H., **Taub**, D., and **Wendler**, N. L. Proton magnetic resonance shifts in steroid D-homoannulation, 214.
**Trevalian**, P. A. See **Brivati**, J. A., 66.
**Trippett**, S. See **Gough**, S. T. D., 302.
**Trotter**, J. *X*-Ray study of a dichloronaphthalene, 78.
**Trotter**, J. See **Brown**, W. A. C., 115; **Hargreaves**, A., 122; **Mak**, T. C. W., 163.
**Truter**, M. R. See **Luxmoore**, A. R., 466; **Swallow**, A. G., 166.
**Turco**, A., **Pecile**, C., and **Niccolini**, M. Bonding of the selenocyanate ion in complexes with cobalt(II), 213.
**Turner**, D. W. See **Glasel**, J. A., 426.
**Tyler**, J. K. See **Brown**, J. K., 13.
**Tyrrell**, H. J. V., and **Firth**, J. G. Thermal diffusion in solutions of carbon tetrachloride in benzene, 201.

V

**Vaughan**, J. See **Fischer**, A., 369.
**Venanzi**, L. M. See **Mair**, G. A., 170.
**Venkatesan**, K. See **Huber-Buser**, E., 463.
**Vernon**, J. M. See **Acheson**, R. M., 164.
**Villotti**, R. See **Djerassi**, C., 450.
**Viswanathan**, N. See **Gopinath**, K. W., 446.
**Vlček**, A. A., and **Rusina**, A. Reduction of aromatic nitro-compounds by sodium borohydride catalysed by transition-metal complexes, 161.
**von Philipsborn**, W. See **Battersby**, A. R., 413.
**Vos**, A. See **Bärnighausen**, H., 120.

W

**Waddington**, T. C. See **Holliday**, A. K., 220.
**Waight**, E. S., and **Weinstock**, M. Preparation and rearrangement of (+)-1-phenylallyl chloride, 334.
**Walker**, A. See **Addison**, C. C., 242.
**Wang**, Chi-Hua. Decomposition of quinone azine: a new carbene, 309.
**Weale**, K. E. See **Stewart**, J. M., 389.
**Weedon**, B. C. L. See **Davis**, J. B., 261.
**Weinstock**, M. See **Waight**, E. S., 334.
**Weir**, N. G. See **Overton**, K. H., 211.
**Wendler**, N. L. See **Trenner**, N. R., 214.
**Weston**, M. See **Ayscough**, P. B., 244.
**Whalley**, W. B. See **Holker**, J. S. E., 464.
**White**, J. D. See **Bonnett**, R., 119.
**White**, P. Surface photolysis experiments on evaporated metal films, 337.
**Whitear**, A. L. See **Praill**, P. F. G., 112.
**Whitear**, B. See **Cookson**, R. C., 117.
**Whitham**, G. H. Solvolysis of the toluene-*p*-sulphonate of 3β-hydroxymethyl-A-norcholest-5-ene, 422.
**Whitham**, G. H. See **Hurst**, J. J., 116.
**Whiting**, D. A. See **Crombie**, L., 19.
**Whittaker**, N. See **Openshaw**, H. T., 454.
**Wieczorkowski**, J. See **Frank**, W., 449.
**Wildman**, W. C. See **Battersby**, A. R., 243; **Gopinath**, K. W., 446.
**Wilkinson**, G. Hydride-ion substitution in metal complexes, 72.
**Williams**, G. H. See **Corbett**, G. E., 240.
**Williams**, R. J. P. See **Crabtree**, J. M., 336.
**Williams**, R. O. See **Berkoff**, C. E., 312.
**Wilson**, D. V. See **Shaw**, G., 381.
**Wilson**, R. See **Ayscough**, P. B., 16.
**Winstein**, S. See **Ledwith**, A., 241.
**Wojcicki**, A. See **Addison**, C. C., 202, 306.
**Wood**, H. C. S. See **Rowan**, T., 260.
**Wood**, J. S. See **Nyburg**, S. C., 297.
**Wright**, D. Preparation of cohulupone from colupulone, 315.
**Wright**, G. J. See **Fischer**, A., 369.
**Wylie**, A. See **Overton**, K. H., 211.

Y

**Yeowell**, D. A. See **Battersby**, A. R., 17, 412, 413; **McPhail**, A. T., 223.
**Yule**, K. C. See **Schwarz**, J. C. P., 417.

Z

**Závada**, J., and **Sicher**, J. Addition of bromine to *trans*- and *cis*-cyclodecene: a transannular reaction, 199.

# COMMUNICATIONS TO PROCEEDINGS: INDEX OF SUBJECTS, 1961

The following index relates to Scientific Communications published in *Proceedings of The Chemical Society*, 1961.


A

**Acetic acid,** dimeric, structure in aqueous solution, 73.
**Acetic anhydride** and analogous compounds, acid-catalysed self-condensation of, 112.
**Acetoxylation** accompanying nitration with nitric acid–acetic anhydride mixtures, 369.
**Acetylene,** monofluoro- and monoiodo-, infrared spectra, 13.
**Acetylenes,** new prep., 302.
photo-addition to benzene, prep. of cyclo-octatetraenes by, 333.
**Acetylenic bonds,** new synthesis, and biosynthetic implications, 245.
**Acids,** α-hydroxyamino-, α-amino-acids and α-keto-acid oximes from, 375.
**Acrylonitrileiron,** tetracarbonyl-, crystal structure, 466.
**Adsorption** of hydrocarbons on a silica–alumina catalyst, study by electron-spin resonance, 70.
**Alcohol–hydrogen chloride systems,** hydrogen dichloride ($HCl_2^-$) ion as a reagent in, 467.
**Alkaloids,** of the Amaryllidaceae, biosynthesis, 243, 254.
of calabash curare, 17, 223, 412, 413.
calycanthaceous: chimonanthine, 465.
diterpenoid, hetero-ring of, 461.
**Alkyl radicals** in γ-irradiated alkyl halides, electron-spin resonance spectra, 247.
**Allenes,** addition of carbenes to, 246.
cyclic, prep., 143.
**Allyl chloride,** (+)-1-phenyl-, prep. and rearrangement, 334.
**complexes,** σ-bonded, unusual protonation reaction of, 378.
**vinyl ethers,** gas-phase Claisen rearrangement of, mechanism, 141.
**Aluminium,** complex pseudohalides of, prep., 203.
chloride, interaction with aromatic hydrocarbons, 142.
**Amaryllidaceae** alkaloids, biosynthesis, 243, 254.
**Amines,** liquid, nuclear magnetic resonance study of hydrogen bonding in, 118.
**Anthracene–tetracene mixed crystals,** intermolecular interactions in, 253.
**Arbuzov rearrangement,** anti-, 12.
**Aromatic compounds,** biosynthesis from acetyl- and malonyl-coenzyme A, 209.
free-radical alkylation and aroylation of, induced by gamma-radiation, 212.
**Arsenic:** Tertiary arsine chelate group, olefinic, complexes involving, 220.
Tertiary arsine–halogen adducts, 65.
**Arylation and aroylation** of aromatic compounds, free-radical, induced by gamma-radiation, 212.
**Arylmethyl** ions, electronic spectra, 386.
**Ascaridole,** reduction with ferrous sulphate solution, 83.
**Atisine,** stereochemistry of the E- and F-rings: relation to the atisine–isoatisine isomerisation, 14.
**Azulene,** electronic excitation in, 11.

B

**Benzene,** derivatives of, Dewar structures as intermediates in, prep., 312.
1,3,5-trimethoxy-, kinetics and equilibria of protonation in concentrated aqueous acid, 81.
nitro-, carbon-basicity of halide and halogenoid ions in, 371.
nitro-, nature of first absorption band of, 171.
**Benzhydryl chloride,** *p*-chloro-, racemization and radio-chloride exchange with mercuric chloride, 241.
**Benzoic acids,** substituted, steric effects in, 162.
**Benzophenone,** photochemical reduction, 301.
**Beryllium,** coloured bipyridyl complexes of, 376.
nitrate, basic, structure, 242.
**Biosynthesis:** Amaryllidaceae alkaloids, 243, 254.
Chrysanthemum-monocarboxylic acid, 452.
Implications of a new synthesis of acetylenic bonds, 245.
**Biphenyl,** crystalline, structure, 122.
**Biphenylene,** structure, 163.
**Bipyridyl** complexes of beryllium, coloured, 376.
**π-Bonding** and hindered rotation in inorganic systems, 421.
**Borazoles,** unsymmetrically substituted, and bicyclic derivatives thereof, 425.
**Born-5-en-2-one,** 5-phenyl-, intensification of absorption and rotation of the carbonyl chromophore in absorption spectrum, 423.
**Boron,** complex pseudohalides of, prep., 203.
organic compounds of, polymer from reaction with diazomethane, end groups in, 117.
Hexachlorodiborate anion, $B_2Cl_6^{2-}$, 220.
Phosphinoborine derivatives, dimeric, prep., 432.
**Bromination,** allylic, by *N*-bromosuccinimide, mechanism, 80, 199.
**Bromine,** addition to *trans*- and *cis*-cyclodecene, 199.
**Bufotenin,** dehydro-, structure, 310.
**Butoxy.** See t-Butoxy.
**Butyl.** See also t-Butyl.
**n-Butyl radicals,** dimerisation and disproportionation of, 18.

C

**Cactus,** sterol (peniocerol) from, structure, 450.
**Calabash curare,** alkaloids from, 17, 223, 412, 413.
**Calythrone,** prep., 374.
**Camphane,** (−)-2-bromo-2-nitro-, stereochemistry, 306.
**Caracurine-II** (alkaloid of calabash curare), 412, 413.
structure, 416.
**Carbene,** a new, formed by decomposition of quinone azine, 309.
ethoxycarbonyl-, reactions of, steric discrimination in, 443.
**Carbenes,** addition to allenes, 246.
**Carbon tetrachloride,** solutions in benzene, thermal diffusion in, 201.
**Carbonium ions,** alkyl and double-bond, electronic spectra, 256.
**Carbonyl chromophore,** intensification of absorption and rotation by mixing $n \longrightarrow \pi^*$ with $\pi \longrightarrow \pi^*$ transitions, 423.
**Carbonyls,** metal, fluorocarbon derivatives of, 69.
**Carbonylation** of platinum and palladium organo-complexes, 67.
**ζ-Carotene,** structure, 261.
**Catalysts,** anionic, catalytic action of, 339.
**Cedrelone** (a triterpene), structure, 444, 446.
**Cephalosporin $P_1$** (antibiotic), 257.
**Chain inhibition** of a non-chain reaction, 301.
**Charge-transfer bonds** in solids: crystal structure of oxalyl bromide, 343.
**Chimonanthine,** a new calycanthaceous alkaloid, 465.
**Chlorine** atoms, abstraction from gaseous t-butyl hypochlorite by methyl radicals, 338.
Chloride, radio-, exchange between *p*-chlorobenzhydryl chloride and mercuric chloride, 241.

**Cholest-5-ene,** 3β-hydroxymethyl-A-nor-, toluene-*p*-sulphonate, solvolysis, 422.
**Cholest-8-ene-3β,6α-diol,** from cactus, 450.
**Chrysanthemum-monocarboxylic acid,** biosynthesis, 452.
**Claisen rearrangement** of allyl vinyl ethers, gas-phase, mechanism, 141.
**Clerodin,** structure, 75.
constitution, 76.
**Cobalt:** Complexes of type $[Co_3(CO)_9(CY)]$, prep. and structure, 169.
Cobalt(II), bonding of the selenocyanate ion in complexes with, 213.
Cobalt(II), tetrahedral and bridged octahedral complexes of, 372.
Cobalt(II) ions, rate of association of thiocyanate ions with, 380.
**Coenzyme A,** acetyl- and malonyl-, biosynthesis of aromatic substances from, 209.
**Cohulupone,** prep. from colupulone, 315.
**Columbin,** stereochemistry, 211.
**Colupulone,** prep. of cohulupone from, 315.
**Complexes,** of the early cations of the first transition series, stability constants of, 336.
of olefins with palladium(II) chloride, reaction with nucleophiles: a new vinylation, 370.
metal, perchlorate co-ordination in, 335.
tervalent-metal, application of high-speed digital computers to the calculation of formation constants for, 340.
**Computers,** high-speed digital, application to calculation of formation constants for tervalent-metal complexes, 340.
**Conessine,** prep., 206.
**Copper:** Copper(II), so-called trico-ordinated complexes of, anomalous magnetic behaviour and binuclear structure, 264.
Cupric dithizonate, primary, crystal structure, 203.
Cupric halides, reactions with aromatic hydrocarbons, 307.
**Corrole,** derivatives of, prep., amendment, 168.
**Crystal field stabilisation** as a factor in surface processes, 424.
**Crystals,** mixed- anthracene–tetracene, intermolecular interactions in, 253.
(±)-**Cuparene,** prep., 74.
**Cyclic systems,** orientation in some elimination reactions, 314.
**Cyclobutene,** 3,4-dimethylene-, prep., 332.
**Cyclodecane** ring, conformation, 463.
*trans-* and *cis-*, addition of bromine to, 199.
**Cyclohexane** and related molecules, ring inversion in, studied by nuclear magnetic resonance, 418.
**Cyclohexylammonium salts,** trimethyl-2-methyl-, eliminations from, orientation in, 314.
**Cyclo-octatetraenes,** prep. by photo-addition of acetylenes to benzene, 333.
**Cyclopentadienide anion** that is stable in water, 117.

D

**Decalin,** *cis-* and *trans*-perfluoro-, from fluorination of tetralin, 138. Nuclear magnetic resonance spectra, 139.
*trans*-**Decalin,** 10-acetyl-1α-halogeno-, reactions of: evidence for an unusual neighbouring-group effect, 451.
**Dewar structures** as intermediates in prep. of benzene derivatives, 312.
**Diazomethane,** monomethylenation and polymethylenation by, in the presence of boron compounds, 172.
**Diazotisation** at intermediate acidities, mechanisms, 173.
**Diels–Alder addition,** gas-chromatographic study of rate, 316.
**Dissymmetry,** molecular, due to symmetrically placed hydrogen and deuterium, 333.
**Diterpenoid alkaloids,** hetero-ring of, 461.
**Dithizone:** Cupric dithizonate, primary, crystal structure, 203.

E

**Echitamine,** reactions, 62.
structure, 63.
**Elimination** and substitution, merged, mechanism, 252.
**Elimination** reaction, novel base-catalysed (conversion of an amide into a cycloheptatrienone), 248.
reactions in cyclic systems, orientation in some, 314.
**Esters,** β-keto-, reaction with hydroxylamine, 387.
**Ethers,** allyl vinyl, mechanism of gas-phase Claisen rearrangement of, 141.
**Ethyl radicals,** kinetics of addition to vinyl monomers, 259.
reaction with isopropyl radicals, 68.
chloro-, excited ($C_2H_xCl_{5-x}$*), 244.
**Eucarvone,** photoisomerisation to 1,5,5-trimethylnorborn-2-en-7-one, 116.

F

**Flavan derivatives,** stereochemistry and conformation, 165.
**Fluorine:** "Halogen monofluorides", addition to fluoro-olefins, 113.
Metal carbonyls, fluorocarbon derivatives, 69.
Perfluoroalkylnitroso-compounds, prep. from perfluoroacyl nitrites, 64.
Polysulphuryl fluorides, 428.
**Formates,** irradiated, radicals in, 66.
**Formation constants** for tervalent-metal complexes, application of high-speed digital computers to calculation of, 340.
**Fumagillin** (an antibiotic), configuration, 331.

G

**Germanium:** Germanes, volatile, prep. and identification, 379.
Germane, mono- and di-fluoro-, prep., 205.
Germyl fluoride, microwave spectrum, 456.
L-**Glucose,** 3-amino-3,6-dideoxy-, derivatives of, 255.

H

**Halide and halogenoid ions** in nitrobenzene, carbon-basicity of, 371.
"**Halogen monofluorides**", addition to fluoro-olefins, 113.
**Hofmann elimination,** ylide mechanism in, 458.
**Hofmann** *versus* **Saytzeff elimination** in the interaction of t-pentyl chloride and acetyl chloride, 382.
**Hydrides,** inorganic complex, solvent effects in the infrared spectra of, 431.
**Hydride-ion** substitution in metal complexes, 72.
**Hydrocarbons,** adsorption on a silica–alumina catalyst, study by electron-spin resonance, 70.
**aromatic,** use of magnesium compounds in alkylation of, 245.
interaction with aluminium chloride, 142.
reactions with cupric halides, 307.
**Hydrocarbon-sulphonyl radicals,** trapped, electron-spin resonance investigation, 71.
**Hydrogen bonding,** in gaseous mixtures, infrared detection: origin of broad bands, 121.
in the hydrogen malonate ion, 373, 464.
in liquid amines, nuclear magnetic resonance study, 118.
**dichloride** ($HCl_2^-$) ion as a reagent in alcohol–hydrogen chloride systems, 467.
**exchange,** of 1,3,5-trimethoxybenzene in concentrated aqueous acid, kinetics and equilibria, 81.
aromatic, and other proton transfer reactions, $H_0$ function and general acid catalysis in, 453.
**Hydroxide and thiophenoxide ions,** relative thermodynamic affinities for carbon, 305.
**Hydroxylamine,** reaction with β-keto-esters, 387.

I

**Ion-exchanger** of new type, fractionation of ribonucleic acids by, 78.
**Iron:** Tetracarbonylacrylonitrileiron, crystal structure, 466.
**Isobutene,** chain-transfer by anisole in cationic polymerisation of, 311.

XUM

**Isoindoline**, 1,3,4,7-tetramethyl-, novel prep. by reductive condensation of 2,5-dimethylpyrrole, 119.
**Isopropyl radicals**, reaction with ethyl radicals, 68.

K

$K_2$, ionisation potential, and rotational analysis of the $C^1\Pi_u$–$X^1\Sigma_g^+$ system of, 329.

L

**Linderone** and methyl-linderone, structures, 455.
**Lithium aluminium hydride reductions**, stereospecificity, 388.
**Lycorine**, incorporation of norbelladine into, 243.

M

**Macusine-A**, structure, 223.
**Macusine-B**, structure, 17.
**Magnesium compounds**, use in alkylation of aromatic hydrocarbons, 245.
**Malonic acid**, acid ion, hydrogen bonding in, 373, 464.
**Manganese**: Nitratopentacarbonylmanganese(I), prep., 202.
**Maytenone**, pyrolytic decomposition: a model system, 265.
**Menschutkin reaction**, reverse, transition-state volume change in, 389.
**Mercury electrode**, anodic capacity in aqueous sodium fluoride solutions, 239.
**Metals**, complexes of, hydride-ion substitution in, 72.
evaporated films of, surface photolysis on, 337.
**transition**, nitrites of, prep., 306.
**Methane**, tetradeutero-, measurement of vibrational relaxation time of, 114.
nitroso-, vapour-phase addition of methyl radicals to, 204.
**Methyl**, triphenyl-, electron-spin resonance spectrum, 16.
**groups**, internal rotation of, as detected by band contours in infrared spectra of solutions and gases, 420.
in aromatic positive ions, hyperfine interactions from, 384.
**ions**, aryl-, electronic spectra, 386.
**radicals**, addition to nitrosomethane in the gas phase, 204.
**Methylation**, homolytic aromatic, 240.
**Monolayers**, oriented, molecular interactions in, observed by infrared spectroscopy involving total internal reflection, 461.
**Mycaminose**, prep. and stereochemistry, 430.

N

**Naphthalene**, a dichloro-, *X*-ray study, 78.
**Naphthalenes**, triaza-, three new, prep., 459.
**Neurosporene**, structure, 261.
**Nickel**: Nickel(II) complexes, Lifschitz, solution spectra and crystal structure, 297.
Nickel(II) ions, rate of association of thiocyanate ions with, 380.
**Nitration** with nitric acid–acetic anhydride mixtures, acetoxylation accompanying, 369.
**Nitro-compounds**, aromatic, reduction by sodium borohydride catalysed by transition-metal complexes, 161.
**Nitrogen**: Dinitrogen tetroxide, $\sigma$-electron delocalisation and electronic structure, 216.
Nitrites, perfluoroacyl, prep. of perfluoroalkylnitroso-compounds from, 64.
Nitrites of transition metals, prep., 306.
**Nitroso-compounds**, perfluoroalkyl-, prep. from perfluoroacyl nitrites, 64.
**Norbelladine**, incorporation into lycorine and norpluvine, 243.
**Norborn-2-en-7-one**, 1,5,5-trimethyl-, photoisomerisation of eucarvone to, 116.
**Norcarane-7-carboxylic acid**: steric discrimination in reactions of ethoxycarbonylcarbene, 443.
**Norpluvine**, incorporation of norbelladine into, 243.
**Nucleoside**, crystalline, isolation from the vitamin $B_{12}$ coenzyme, 447.
**Nucleosides**, sulphonium, alkali hydrolysis of, 449.

O

**Olefins**, fluoro-, addition of " halogen monofluorides " to, 113.
**Olefin–palladium(II) chloride complexes**, reaction with nucleophiles: a new vinylation, 370.
**Oxalates**, irradiated, radicals in, 66.
**Oxalyl bromide**, crystal structure, 343.

P

**Palladium**, organo-complexes of, carbonylation, 67.
Palladium(II) chloride–olefin complexes, reaction with nucleophiles: a new vinylation, 370.
**Penicillic acid**, rôle of acetate and malonate in biosynthesis of, 111.
**Peniocerol**, sterol from cactus, structure, 450.
**Pentyl**. See t-Pentyl.
**Perchlorate co-ordination** in metal complexes, 335.
**Perylene**, 1,12-*o*-phenylene-, crystals isolated during prep., *X*-ray study, 115.
**Phenalenyl radical**, detection in pyrolysed hydrocarbons by electron-spin resonance, 144.
**Phosphazenes**, alkoxy-, rearrangement, 258.
**Phosphorus**: Phosphinoborine derivatives, dimeric, prep., 432.
Phosphinothiolic acid, ethylphenyl-, optical resolution, 145.
Phosphorane, methoxycarbonylmethylenetriphenyl-, reaction with hindered ketones, 454.
**Photolysis**, surface, on evaporated metal films, 337.
**Phytoene**, structure, 261.
**Phytofluene**, structure, 261.
**Platinum**, five-co-ordinated compound of, stereochemistry, 170.
organo-complexes of carbonylation, 67.
Bipyridyl-(1-acetylacetonyl)trimethylplatinum(IV), structure, 166.
**Podophyllotoxin**, stereospecificity of reduction with lithium aluminium hydride, 388.
**Polymerisation**, cationic, of isobutene, chain-transfer by anisole in, 311.
cationic, of styrene, transfer mechanisms in, 460.
**Polysaccharides**, application of the Weermann reaction to, 300.
**Potassium**: $K_2$, ionisation potential, and rotational analysis of the $C^1\Pi_u$–$X^1\Sigma_g^+$ system of $K_2$, 329.
**Proton transfer reactions**, $H_0$ function and general acid catalysis in, 453.
**Protonation** of 1,3,5-trimethoxybenzene in concentrated aqueous acid, kinetics and equilibria, 81.
**Pteridines**, 8-substituted, nucleophilic additions of, and their biochemical significance, 260.
**Pyrrole**, 2,5-dimethyl-, reductive condensation of: novel isoindoline prep., 119.
**Pyrroles**, 1-alkyl-, new type of addition to, 164.

Q

**Quinolizidine** stereochemistry, 218.
**Quinone azine**, decomposition to give a carbene, 309.
**Quinoxalinecarboxyanilides**, rearrangement of, 167.

R

**Radicals** in irradiated formates and oxalates, 66.
**1-β-D-Ribofuranosylimidazole-4-carboxylic acid 5′-*O*-phosphate**, 5-amino-, prep., 381.
**Ribonucleic acids**, fractionation by a new type of exchanger, 78.
**Ring inversion** in cyclohexane and related molecules, studied by nuclear magnetic resonance, 418.
**Rotation**, hindered, and $\pi$-bonding in inorganic systems, 421.
**Rotenoids**, determination of geometry of B/C fusion by means of long-range asymmetric magnetic shielding of the carbonyl group, 299.
reactions of, prefaced by alkaline attack, 19.
**Ruthenium**: Nitratonitrosylruthenium complexes, 251.

S

**Selenium:** Selenocyanate ion, bonding in complexes with cobalt(II), 213.
**Semiquinones,** electron-spin resonance spectra in sulphuric acid, 385.
**Shifts,** chemical, of nitrogen-14 nuclei bonded to protons, measurement by nuclear magnetic double resonance, 303.
**Sodium borohydride,** reduction of aromatic nitro-compounds by, catalysed by transition-metal complexes, 161.
**Solvolysis** by $S_N$ mechanisms, entropies and heat capacities of activation in, 222.
**Spectra:**
**absorption:** carbonyl chromophore, intensification of absorption by mixing of $n \longrightarrow \pi^*$ and $\pi \longrightarrow \pi^*$ transitions, 423.
Lifschitz nickel(II) complexes in solution, 297.
nitrobenzene, nature of first (absorption) band, 171.
**electron-spin resonance:** alkyl radicals in $\gamma$-irradiated alkyl halides, 247.
hydrocarbons, study of adsorption on a silica–alumina catalyst, 70.
hydrocarbons, aromatic, study of interaction with aluminium chloride, 142.
hydrocarbon-sulphonyl radicals, trapped, investigation of, 71.
methyl, triphenyl-, 16.
phenalenyl radical, detection in pyrolysed hydrocarbons, 144.
semiquinones in sulphuric acid, 385.
sulphur nitride ions, 377.
*p*-xylene positive ion, 174.
**electronic:** arylmethyl ions, 386.
**infrared:** acetylene, monofluoro- and monoiodo-, 13.
hydrides, inorganic complex: solvent effects, 431.
hydrogen bonding in gaseous mixtures: detection, and origin of broad bands, 121.
metal–chlorine stretching frequencies, infrared active, 335.
methyl groups, internal rotation detected by band contours in spectra of solutions and gases, 420.
monolayers, oriented, observations of molecular interactions in, by infrared spectroscopy involving total internal reflection, 461.
thiocyanic acid in solution, rotational structure of a bending vibration, partial resolution, 342.
**microwave:** germyl fluoride, 456.
**nuclear magnetic resonance:** amines, liquid, hydrogen bonding in, 118.
cyclohexane and related molecules, ring inversion in, 418.
dehydrobufotenin " hydrochloride ", 310.
*cis*- and *trans*-perfluorodecalin, 139.
Shifts, chemical, measurement by double-resonance, 303.
Spin decoupling and relative chemical shifts of dissimilar nuclei measured by using frequency related oscillators, 426.
steroid D-homoannulation (proton magnetic resonance shifts), 214.
thallium trialkyls, proton magnetic resonance, 208.
**ultraviolet:** carbonium ions, alkyl and double-bond, 256.
**Stability constants** of some complexes of the early cations of the first transition series, 336.
**Steroid D-homoannulation,** proton magnetic resonance shifts in, 214.
**Steroid 3-ketones,** 4,4-dimethyl-, conformation of ring A in some, 464.
**Steroids,** 5,9-cyclo-, prep., 207.
**$\Delta^4$-Steroids,** 4-methyl-3-oxo-, new route to, 114.
**Styrene,** cationic polymerisation of, transfer mechanisms in, 460.
polymerisation by perchloric acid, 200.
**Substitution,** and elimination, merged, mechanism, 252.
nucleophilic aromatic, transition state in, 341.
**Succinic anhydrides,** catalytic hydrogenation of, 313.
**Sugars,** amino-, sulphur substitution compounds of. Part III, 429.
with sulphur in the ring, 417, 418.
**Sulphur,** in ring of sugars, 417, 418.
nitride, ions, electron-spin resonance spectra, 377.
Disulphoxide and thiolsulphonate formulations, chemical distinction between, 250.
Polysulphuryl fluorides, 428.
Thiolsulphonates, structure, and chemical distinction between disulphoxides and, 250.
**Sultones,** unsaturated, irradiation of, 238.
**Surface processes,** crystal field stabilisation as a factor, 424.
**Sydnone,** structure of a, 120.

T

**L-Talose,** 3-amino-3,6-dideoxy-, derivatives of, 255.
**t-Butoxy-group,** novel hydroxyl-protecting group in peptide synthesis with hydroxy-amino-acids, 249.
**t-Butyl hypochlorite,** gaseous, abstraction of chlorine atoms by methyl radicals, 338.
**Tetracene–anthracene mixed crystals,** intermolecular interactions in, 253.
**1-Tetralone,** 2-benzyl-2-bromo-4,4-dimethyl-, decomposition, mechanism of merged substitution and elimination, 252.
**Thallium trialkyls,** proton magnetic resonance spectra, 208.
**Thiocyanic acid** in solution, partial resolution of the rotational structure of a bending vibration, 342.
Thiocyanate ions, rates of association with nickel(II) and cobalt(II) ions, 380.
**Thiolsulphonates,** structure and chemical distinction between disulphoxides and, 250.
**Thiophenoxide** and hydroxide ions, relative thermodynamic affinities for carbon, 305.
**Thiourea** as a leaving group from carbon in $S_N$ displacements, 214.
**Tin:** Dialkyltin(IV) compounds, structure of intermediates in hydrolysis of, 457.
Distannoxanes, dimerisation by co-ordination, 383.
Stannite ion, trichloro-, pyramidal configuration, 304.
**t-Pentyl chloride,** Hofmann *versus* Saytzeff elimination in the interaction with acetyl chloride, 382.
**Transition series,** first, stability constants of some complexes of the early cations of, 336.
**Triterpenoid 3-ketones,** conformation of ring A in some, 464.

V

**Vinyl** allyl ethers, gas-phase Claisen rearrangement of, mechanism, 141.
**Vinyl monomers,** kinetics of addition of ethyl radical to, 259.
**Vinylation,** new: reaction of olefin–palladium(II) chloride complexes with nucleophiles, 370.
**Vitamin $B_{12}$ co-enzyme,** crystalline nucleoside isolated from, 447.

W

**Wave functions,** molecular, new method for deriving, 427.
**Weermann reaction,** application to polysaccharides, 300.
**DL-Willardiine,** prep., 216.

X

***p*-Xylene** positive ion, electron-spin resonance spectrum, 174.
**D-Xylothiapyranose:** a sugar with sulphur in the ring, 417.

Y

**Ylide mechanism** in Hofmann elimination, 458.

Z

**Zierone,** constitution, 308.


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